KEY CHARACTERISTICS OF MYELOFIBROSIS (MF)1–7

- MF is a serious hematologic malignancy characterized by multiple genetic, epigenetic and cellular alterations1–3
- Diagnosis is made with a combination of laboratory analyses and clinical patient evaluation4
- Overactive JAK signaling, and not only the JAK2V617F mutation, is the underlying driver of the disease5–7
- Splenomegaly is a sign of extramedullary hematopoiesis and can cause significant burden for the patient, leading to further complications1

HOW DO THE INTERNATIONAL PROGNOSTIC SCORING SYSTEM (IPSS) RISK FACTORS AFFECT MEDIAN SURVIVAL?2

Several scoring systems have been validated for estimating prognosis in MF. IPSS is used for risk stratification at the initial diagnosis of PMF.2

International Prognostic Scoring System (IPSS)2
Used for risk stratification at initial diagnosis

- Age >65 years
- Presence of constitutional symptoms
- Hemoglobin <10 g/dL
- White blood cell count > 25 x 10⁹/L
- Blood blasts ≥1%

### Diagnosis of PMF Based on WHO Criteria

Check the major and minor criteria corresponding to a patient’s clinical presentation. Add the number of check marks in the highlighted criteria in each column and compare the result against the totals required to meet WHO guidelines for diagnosis of PMF.

<table>
<thead>
<tr>
<th>Source</th>
<th>Criteria</th>
<th>Major Criteria</th>
<th>Minor Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical examination</td>
<td>Palpable splenomegaly</td>
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<tr>
<td>Bone marrow biopsy</td>
<td>Proliferation and atypia of megakaryocytes, with or without reticulin and/or collagen fibrosis*</td>
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<tr>
<td>Complete blood count</td>
<td>Anemia</td>
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<tr>
<td>Biochemistry</td>
<td>Increased serum LDH</td>
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<tr>
<td>Blood film (smear)</td>
<td>Leukoerythroblastosis</td>
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</table>

**Total Number of Highlighted Criteria**

To meet WHO diagnostic criteria for this MPN

*Must have at least*

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<tbody>
<tr>
<td>3</td>
<td>2</td>
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</tbody>
</table>

**CML** = chronic myelogenous leukemia; **EPO** = erythropoietin; **LDH** = lactate dehydrogenase; **MDS** = myelodysplastic syndrome; **MPN** = myeloproliferative neoplasm; **PV** = polycythemia vera; **WHO** = World Health Organization

*Presence of megakaryocyte proliferation and atypia (small to large megakaryocytes with an aberrant nuclear/cytoplasmic ratio and hyperchromatic, bulbous, or irregularly folded nuclei and dense clustering). In the absence of significant reticulin fibrosis, the megakaryocyte changes must be accompanied by an increased bone marrow cellularity characterized by granulocytic proliferation and often decreased erythropoiesis (i.e., prefibrotic cellular-phase disease).*
IDENTIFYING PATIENTS WITH POST-PV MF AND POST-ET MF

PV and ET progress to MF at a rate of 10% and <4% over 10 years, respectively. Careful monitoring of patients with PV and ET can facilitate early identification of disease progression to Post-PV MF and Post-ET MF.

Check off the major and minor criteria corresponding to a patient’s clinical presentation. Add the number of check marks in the HIGHLIGHTED criteria in each column and compare the result against the totals required to meet IWG-MRT guidelines for diagnosis of Post-PV MF and Post-ET MF.

<table>
<thead>
<tr>
<th>Source</th>
<th>Criteria</th>
<th>POST-PV MF</th>
<th>POST-ET MF</th>
<th>Major criteria</th>
<th>Minor criteria</th>
<th>Major criteria</th>
<th>Minor criteria</th>
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<tbody>
<tr>
<td>Patient history</td>
<td>Previous diagnosis of WHO-defined PV</td>
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<td>Previous diagnosis of WHO-defined ET</td>
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<td>☐</td>
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<tr>
<td>Clinical examination</td>
<td>Increasing splenomegaly&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>Development of at least 1 of the following constitutional symptoms: &gt;10% weight loss in 6 months, night sweats, or unexplained fever</td>
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<tr>
<td>Bone marrow biopsy</td>
<td>Bone marrow fibrosis&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>Complete blood count</td>
<td>Anemia&lt;sup&gt;c&lt;/sup&gt;</td>
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</tbody>
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**TOTAL NUMBER OF HIGHLIGHTED CRITERIA** ☐ ☐

To meet IWG-MRT diagnostic criteria for this MPN » Must have at least » ☐ ☐ 2 ☐ 2

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ET = essential thrombocythemia; IWG-MRT = International Working Group for Myeloproliferative Neoplasms Research and Treatment; LDH = lactate dehydrogenase; PV = polycythemia vera; MPN = myeloproliferative neoplasm; WHO = World Health Organization

<sup>a</sup>Either an increase in palpable splenomegaly of ≥5 cm (distance of the tip of the spleen from the left costal margin) or the appearance of a newly palpable splenomegaly.

<sup>b</sup>Grade 2-3 according to the European classification: diffuse, often coarse fiber network with no evidence of collagenization (negative trichrome stain) or diffuse, coarse fiber network with areas of collagenization (positive trichrome stain). Grade 3-4 according to the standard classification: diffuse and dense increase in reticulin with extensive intersections, occasionally with only focal bundles of collagen and/or focal osteosclerosis or diffuse and dense increase in reticulin with extensive intersections with coarse bundles of collagen, often associated with significant osteosclerosis.

<sup>c</sup>Below the reference range for appropriate age, sex, gender, and altitude. For Post-PV MF, sustained loss of requirement for phlebotomy in the absence of cytoreductive therapy is sufficient. For Post-ET MF, must be accompanied by ≥2 g/dL decrease from baseline hemoglobin level.

<sup>d</sup>Above reference level.
THE DISEASE BURDEN OF MYELOFIBROSIS

THE MAJORITY OF PATIENTS WITH MF ARE AFFECTED BY SPLENOMEGALY AND DISEASE-RELATED SYMPTOMS

MF is a progressive, often debilitating disease with well-documented morbidity and mortality. To better understand the impact on patients, several validated instruments have been developed to measure specific symptoms and severity. One of these tools is the Myeloproliferative Neoplasm Symptom Assessment Form (MPN-SAF).

PREVALENCE OF SYMPTOMS REPORTED IN PATIENTS WITH MF

Prospective, international, multisite cohort of patients with MF (n = 96).

SUMMARY

MF is a progressive, often debilitating disease with significant symptomatic burden. MF develops primarily de novo, but many patients are diagnosed with MF after an initial diagnosis of PV or ET. Early identification of patients with MF is important because it facilitates disease monitoring and informs clinical decision making.

REFERENCES


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