**Testing Algorithm for Myeloproliferative Neoplasms**

**Concern for PV**
- **JAK2 p.V617F**
  - If neg
  - **JAK2 exon 12**
  - If neg
  - Consider CALR, MPL, or panel testing and rethink your diagnosis

**Concern for ET or PMF**
- **JAK2 p.V617F**
  - If neg
  - **CALR (exon 9) and MPL p.W515**
  - If neg
  - Consider panel testing for other diagnostic or prognostic signatures (e.g., ASXL1, TP53)

**Concern for CML**
- Quantitative **BCR/ABL1** at minimum for e13a2 and e14a2
  - If neg
  - **FISH for BCR/ABL1**
  - If neg
  - Consider panel testing and rethink your diagnosis

**Concern for CNL**
- **CSF3R**
  - If neg
  - Consider panel testing for other diagnostic or prognostic signatures (ASXL1, TP53)

**Concern for CEL (vs HES or myeloid/lymphoid neoplasms)**
- **FISH for FIP1L1/PDGFRA, PDGFRB, FGFR1, or PCM1-JAK2**
  - If neg
  - Consider panel testing for other markers of clonality and poor prognostic signatures (e.g., ASXL1, TP53)

**Abbreviations:**
- PV – Polycythemia Vera; ET – Essential Thrombocythemia; PMF – Primary Myelofibrosis; CML – Chronic Myeloid Leukemia; CNL – Chronic Neutrophilic Leukemia; CEL – Chronic Eosinophilic Leukemia; HES – Hypereosinophilic syndrome; MPN – myeloproliferative neoplasm; MDS – myelodysplastic syndrome; RS – ring sideroblast; T – thrombocytosis; VAF – variant allele frequency

**NOTES:**
- Blue lines/box if using only NGS panel testing, green boxes for sequential single gene testing.
- Many of these diagnoses also require proving the absence of BCR/ABL1 by any method.
- A karyotype is also a standard part of the work-up in all cases.
### Genes to Test in Myeloproliferative Neoplasms

**Biomarker**
- **BCR/ABL1**
- **JAK2**
- **CALR**
- **MPL**
- **CSF3R**
- **FIP1L1/PDGFRA**
- **PDGFRB**

**Samples to Test:** Peripheral Blood or Bone Marrow

**Abbreviations:** See Opposite Side of Card

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Specific Alterations/Alternative Terms</th>
<th>Indications</th>
<th>Result Interpretation/Significance</th>
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<tbody>
<tr>
<td>BCR/ABL1</td>
<td>Philadelphia (Ph) Chromosome Usually p210 fusions - e13a2 and e14a2 Rarely p190 fusion - e1a2 or p230 fusion - e19a2 or fusions involving a3</td>
<td>Diagnosis and monitoring of CML Diagnosis of other MPNs and MDS/MPNs which require exclusion of CML by negative BCR/ABL1</td>
<td>Usually p210 fusions - e13a2 and e14a2 Rarely p190 fusion - e1a2 or p230 fusion - e19a2 or fusions involving a3</td>
</tr>
<tr>
<td>JAK2</td>
<td>p.V617F activating hotspot</td>
<td>Diagnosis: p.V617F for first line single gene testing for PV (95%), ET (50-70%), and PMF (30-50%) Exon 12 mutations (~5% of PV)</td>
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</tr>
<tr>
<td>CALR</td>
<td>Exon 9 frameshift mutations</td>
<td>Diagnosis: CALR exon 9 frameshift in ET (25-30%) and PMF (30-35%)</td>
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</tr>
<tr>
<td>MPL</td>
<td>p.W515L activating hotspot</td>
<td>Diagnosis: MPL p.W515L in ET (5%) and PMF (5-10%)</td>
<td>Diagnosis: MPL p.W515L in ET (5%) and PMF (5-10%)</td>
</tr>
<tr>
<td>CSF3R</td>
<td>p.T618I activating hotspot</td>
<td>Diagnosis: CSF3R exon 12 activating substitution mutations</td>
<td>Diagnosis: CSF3R exon 12 activating substitution mutations</td>
</tr>
<tr>
<td>FIP1L1/PDGFRA</td>
<td>Usually cryptic deletion involving CHIC2</td>
<td>Diagnosis: FIP1L1/PDGFRA usually cryptic deletion involving CHIC2</td>
<td>Diagnosis: FIP1L1/PDGFRA usually cryptic deletion involving CHIC2</td>
</tr>
<tr>
<td>PDGFRB</td>
<td>Various fusion partners</td>
<td>Diagnosis: PDGFRB various fusion partners</td>
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</tr>
<tr>
<td>PDGFRB</td>
<td>Exon 18 activating hotspot</td>
<td>Diagnosis: PDGFRB Exon 18 activating hotspot</td>
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<tr>
<td>CSF3R</td>
<td>Exon 9 frameshift mutations</td>
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</tr>
<tr>
<td>CALR</td>
<td>Exon 9 frameshift mutations</td>
<td>Therapy: Therapy response: CALR Exon 9 frameshift mutations</td>
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</tr>
</tbody>
</table>

**Where to Test:** Testing should be performed in the laboratories that are certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) as qualified to perform high complexity molecular pathology testing.

**References:** NCCN Guidelines for Chronic Myeloid Leukemia (v1.2018) and Myeloproliferative Neoplasms (v2.2018)

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