Concern for PV

**JAK2** p.V617F

If neg

**JAK2** exon 12

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

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

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**)

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

**Abbreviations:** PV – Polycythemia Vera; ET – Essential Thrombocythemia; PMF – Primary Myelofibrosis; CML – Chronic Myeloid Leukemia; CNL – Chronic Neutrophilic Leukemia; CEL – Chronic Eosinophilic Leukemia; HES – Hyper-eosinophilic syndrome; MPN – myeloproliferative neoplasm; MDS – myelodysplastic syndrome; RS – ring sideroblast; T – thrombocytosis; VAF – variant allele frequency
# Genes to Test in Myeloproliferative Neoplasms

**Samples to Test:** Peripheral Blood or Bone Marrow  
**Abbreviations:** See Opposite Side of Card

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| **BCR/ABL1**| Philadelphia (Ph) Chromosome  
Usually p210 fusions - e13a2 and e14a2  
Rarely p190 fusion - e1a2 or p230 fusion - e19a2 or fusions involving a3 | Diagnosis and monitoring of CML  
Diagnosis of other MPNs and MDS/MPNs which require exclusion of CML by negative BCR/ABL1  
Therapy: ABL1 kinase inhibitors | Diagnostic of CML in the correct clinical context.  
Also found in some ALLs and AMLs.  
Reported in International Scale (% IS), used for monitoring CML |
| **JAK2**   | p.V617F activating hotspot  
Exon 12 activating substitution mutations | 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)  
Therapy: JAK2 inhibitors | p.V617F not specific for a single disease can be found in a wide range of myeloid neoplasms, associated with thrombosis and erythrocytosis  
High VAF (>75%) is associated with disease progression |
| **CALR**   | Exon 9 frameshift mutations | Diagnosis:  
CALR exon 9 frameshift in ET (25-30%) and PMF (30-35%) | Exon 9 frameshift not specific for a single disease but are useful to support a diagnosis of ET or PMF |
| **MPL**    | p.W515K/L activating hotspot | Diagnosis:  
MPL p.W515K/L in ET (5%) and PMF (5-10%) | p.W515K/L not specific for a single disease but are useful to support a diagnosis of ET or PMF |
| **CSF3R**  | p.T618I activating hotspot  
Other activating substitutions, predominantly exon 17 | Diagnosis:  
CNL (100%), other myeloid neoplasms  
Therapy:  
p.T618I - possible ruxolitinib sensitivity  
p.S783fs* - possible dasatinib sensitivity | Mutated in nearly all cases of CNL as well as in other myeloid neoplasms  
Specific mutations suggest therapy |
| **FIP1L1/PDGFBRA** | Usually cryptic deletion involving CHIC2 | Diagnosis: identify specific subtype of neoplasms  
Therapy response:  
**PDGFBRA/B** fusions are typically responsive to kinase inhibitors such as imatinib  
**FGFR1** fusions are typically non-responsive to imatinib and may need newer agents | Fusions involving **PDGFBRA/B**, **FGFR1**, and **JAK2** are diagnostic of a specific subgroup of lymphoid and myeloid neoplasms with eosinophilia that are considered in a distinct category from MPNs, but may be considered in the differential of CEL |
| **PDGFB/ various partners** | Various fusion partners, most commonly ETV6 | Diagnosis: identify specific subtype of neoplasms  
Therapy response:  
**PDGFBRA/B** fusions are typically responsive to kinase inhibitors such as imatinib  
**FGFR1** fusions are typically non-responsive to imatinib and may need newer agents | Fusions involving **PDGFBRA/B**, **FGFR1**, and **JAK2** are diagnostic of a specific subgroup of lymphoid and myeloid neoplasms with eosinophilia that are considered in a distinct category from MPNs, but may be considered in the differential of CEL |
| **FGFR1/ various partners** | Various fusion partners | | |
| **PCM1-JAK2** | Also includes other partners of **JAK2** (e.g., ETV6 or BCR) | Clonality may be used to support a diagnosis of an MPN in the correct clinical/pathologic context (e.g., triple negative MPNs, CEL vs HES)  
Specific patterns may suggest other entities  
**SF3B1** mutations may suggest MDS-RS or MDS/MPN-RS-T  
**CBL** mutations may suggest CMML | Provides diagnostic information to support single gene testing  
Adds additional prognostic information (e.g., **ASXL1** or **TP53** mutations or high number of mutations portend poor prognosis)  
May suggest pending progression (e.g., **NRAS** mutations, elevated **JAK2** VAF) |

**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)