Panel Approach to Molecular Testing for Suspected MPN Patient Reveals Dual Mutation, Driving Greater Care Insight

Case reviewed by Frank Bauer, MD Medical Director, Precipio Inc.

Abstract:

The evaluation of patients with persistent or marked thrombocytosis includes molecular testing for the presence of underlying myeloproliferative neoplasms (MPN). This has traditionally included testing initially for JAK2 V617F mutation. Reflex testing of other MPN driver mutations; JAK2 Exon 12, Exon 13, MPL and CALR; are only performed if the JAK2 V617F test result is negative. This case study of a patient with a dual mutation of JAK2 V617F & CALR highlights the diagnostic utility and advantages of testing for MPN driver mutations as a comprehensive panel.

Background:

A 72-year-old female presented to her primary care physician with non-specific complaints of dizziness and mild bruising. Routine laboratory testing included a CBC which showed marked thrombocytosis (Platelet Count 911,000). The rest of the CBC was not remarkable. The clinician suspected the possibility of a myeloproliferative neoplasm (MPN), and a blood sample was collected and sent to Precipio's laboratory for a HemeScreen MPN panel.

Case Work Up & Results:

Results of the HemeScreen® MPN panel were as follows:

- ***Positive*** for JAK2 V617F point mutation
- Negative for JAK2 exon 12 mutations
- Negative for JAK2 exon 13 (G571S) mutation
- Negative for MPL W515L/K point mutations
- ***Positive*** for CALR exon 9 insertion/deletion mutations

Analysis:

The advantage of complete panel testing for MPN driver mutations is highlighted by this case. In this patient, the CALR mutation would have been missed if testing had stopped following the positive JAK2 V617 result. An expanding body of literature indicates there is a subset of patients with dual MPN mutations. The co-mutation of JAK2 V617F and CALR genes in this patient has potential impacts on clinical monitoring, treatment, and follow-up molecular testing. Beyond therapeutic implications for JAK2 V617 mutations, CALR mutation in essential thrombocytosis may be associated with an increased clinical risk for CNS hemorrhage and stroke with aspirin treatment and other NSAIDs.

Clinical Implications:

Recent NCCN guidelines suggest that treatment options for this patient will be significantly affected with the additional information of the patient's dual mutation. The chart[1] below details these guidelines.

Diagnosis Provided By Frank Bauer, MD:

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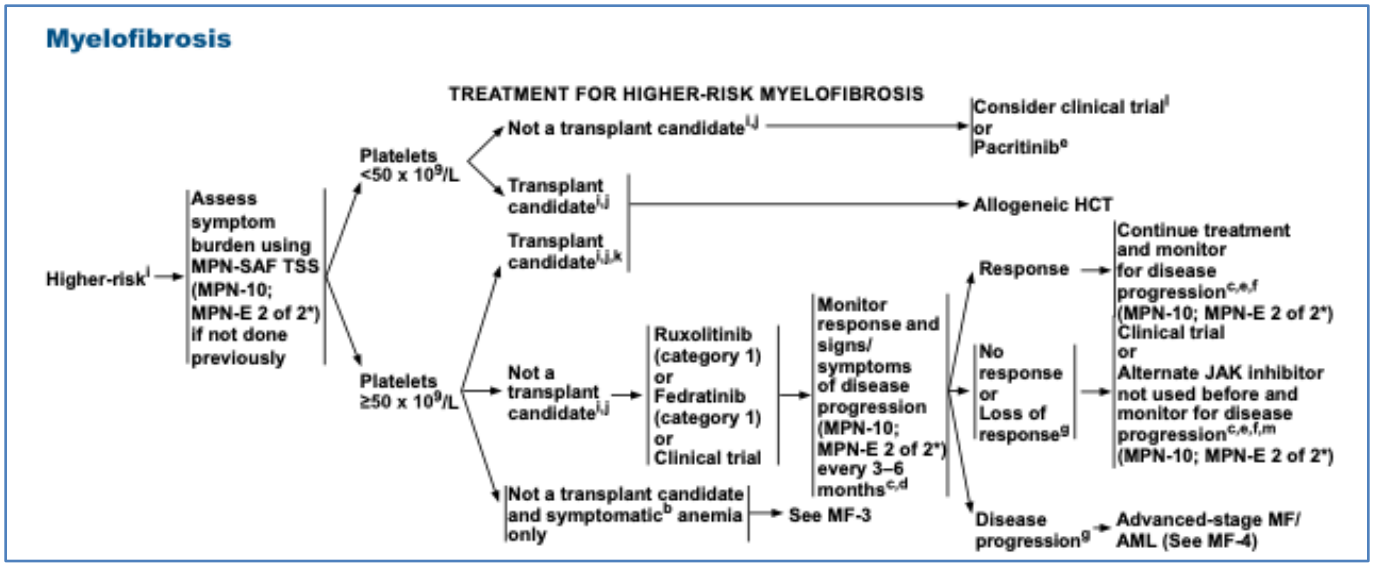

[1] Myeloproliferative Neoplasms, Version 3.2022, NCCN Clinical Practice Guidelines in Oncology