JAK2 V617F Mutation Testing for Non-CML Chronic Myeloproliferative Neoplasms

Background Information

Myeloproliferative neoplasms (MPN) are clonal hematological malignancies characterized by abnormal proliferation of one or more myeloid lineages. One of these disorders, chronic myelogenous leukemia (CML), is defined by the presence of a *BCR-ABL1* translocation, but specific, disease-defining molecular genetic abnormalities for the other typical MPNs (primary myelofibrosis, essential thrombocythemia and polycythemia vera) have not been identified. Therefore, diagnosis has relied on a constellation of clinical and pathologic features as well as exclusion of other specific genetic abnormalities such as *BCR-ABL1* translocation.

Recent studies have shown that a significant number of patients diagnosed with non-CML MPNs have an acquired mutation in *JAK2* (c.1849G>T p.V617F). Estimates of the frequency are variable with the highest percentages seen in polycythemia vera (> 95% of cases). A lower, but still substantial percentage of essential thrombocythemia (40-50%) and primary myelofibrosis (50%) cases also harbor this mutation. *JAK2* V617F is either not found or is extremely uncommon in other disorders such as typical CML, myelodysplastic syndromes, acute leukemias without prior MPNs, acute lymphoblastic leukemias, and chronic lymphocytic leukemia.[1-9]

Clinical Indications

Suspected non-CML myeloproliferative neoplasms or overlap myelodysplastic/myeloproliferative diseases.

Interpretation

The test result is reported as *JAK2* V617F mutation present or absent. In positive cases, the relative mutation burden is also reported in semi-quantitative fashion (i.e., mutant represents minority of detectable alleles vs. mutant represents majority of detectable alleles). The presence of the *JAK2* V617F mutation representing a majority of detectable *JAK2* alleles is consistent with a bi-allelic mutation.

Limitations of the Assay

1. The analytical sensitivity of the assay is approximately 2% mutant alleles. Thus, lower level involvement of the sample (either blood granulocytes or bone marrow) may not be detected, and repeat testing at a later date may be helpful in selected patients.
2. Since the mutation is not disease-specific, correlation with other clinical and laboratory findings is required for subclassification of disease type in the event of a positive (mutation detected) result.
3. Absence of the mutation does not exclude the presence of a myeloproliferative neoplasm.

Methodology

JAK2 V617F mutation analysis is performed using a semi-quantitative, TaqMan allelic discrimination assay (Ipsogen, Marseille, France):

1. DNA is isolated from peripheral blood, bone marrow, or formalin-fixed, paraffin-embedded tissue.
2. PCR for the region of interest is performed, and mutant vs wild type alleles are discriminated using a FAM labeled mutant specific probe and a VIC labeled wild type specific probe.
3. The ratio of mutant to wild type *JAK2* is calculated and compared to control samples containing 2%, 50% or 100% mutant alleles.

References

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Test Overview

Test Name	*JAK2* V617F assay for diagnosis of non-CML CMPD
Specimen Requirements	Peripheral blood, bone marrow aspirate, or formalin-fixed, paraffin-embedded tissue
Billing Code	83623
CPT Codes	81270

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