

MPL W515 Quantitative Mutation Analysis

DETECTS AND QUANTITATES MPL CODON 515 MUTATIONS IN PRIMARY MYELOFIBROSIS (PMF) AND ESSENTIAL THROMBOCYTHEMIA (ET)

Clinical Background

- *BCR-ABL1*-negative chronic myeloproliferative neoplasms include polycythemia vera (PV), essential thrombocytosis (ET), and primary myelofibrosis (PMF).
- More than 50 percent of ET and PMF patients harbor the *JAK2* V617F activating mutation; a subset of ET cases (5–10 percent) have an activating mutation in codon 515 of the thrombopoietin receptor, MPL.
- Mutations in exon 10 of the myeloproliferative leukemia virus oncogene (MPL) are present in approximately 5 percent of patients with PMF and ET.¹
- MPL encodes a transmembrane receptor tyrosine kinase that acts as a receptor for thrombopoietin (TPO), a glycoprotein cytokine responsible for thrombopoiesis. The most common MPL mutations are the W515K and W515L mutations, which have been shown to activate the *JAK/STAT* signaling pathway in the absence of TPO and contribute to the oncogenic phenotype.² The vast majority of patients with *MPL* mutations test negative for the *JAK2* V617F mutation yet possess a phenotype consistent with a myeloproliferative neoplasm.³
- Detection and quantitation of *MPL* mutations can be used in the diagnosis and monitoring of myeloproliferative neoplasms and are suggestive of either PMF or ET in a subset of *JAK2*-unmutated patients.

Indications for Ordering

- Detection of *MPL* mutations in *JAK2*-negative patients with myeloproliferative neoplasms.
- This assay can also be used to monitor for response or clonal expansion in *MPL*-mutated tumors following treatment.

Interpretation

- Not detected: A W515 mutation was not detected.
- Detected: A W515 mutation was detected (percent of mutant allele).

Limitations

- Results of this test must always be interpreted in the context of morphologic and other relevant data, and should not be used alone for a diagnosis of malignancy.
- Samples that do not demonstrate W515 mutations by this test may still have a mutation, but in quantities below the test's limit of detection.
- This test may not accurately detect mutations if present in fewer than 5 percent of granulocytes.

Methodology

- Genomic DNA is purified from enriched granulocytes and subjected to PCR amplification of MPL codon 515 followed by pyrosequencing analysis.
- The ratio of wild-type to W515-mutated alleles is reported.

References

1. Pardanani AD, et al. MPL515 mutations in myeloproliferative and other myeloid disorders: a study of 1182 patients. *Blood* 2006;108:3472–6.
2. Chaligne R, et al. Evidence for MPL W515K/L mutations in hematopoietic stem cells in primitive myelofibrosis. *Blood* 2007;110(10):3735–43.
3. Williams DM, et al. Phenotypic variations and new mutations in *JAK2* V617F-negative polycythemia vera, erythrocytosis, and idiopathic myelofibrosis. *Exp Hematol* 2007;35(11):1641–6.

Test Information

2005545 **MPL codon 515 Mutation Detection by Pyrosequencing, Quantitative**

For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult[®] at www.arupconsult.com.

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