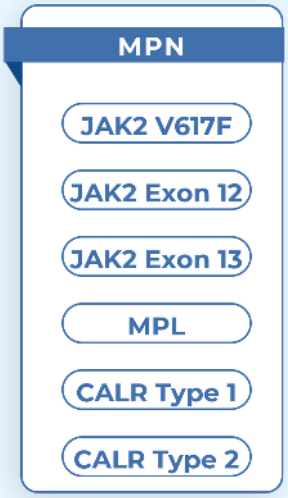
Precipio Spotlight:

Bloodhound MPN Panel Detects JAK2 Exon 13 Mutation Missed by Single Gene Test Method, Enabling Earlier, Less Aggressive, and More Affordable Intervention Options

Case Background

- 46 YO | Male
- Secondary Polycythemia
- Elevated white count
- Suspicious for MPN

Technology Advantage



Bloodhound MPN Panel

More Case Studies

Abstract

Accurate diagnosis and effective treatment of myeloproliferative neoplasms (MPNs) hinges on the identification of driver mutations found in JAK2, MPL, and CALR genes. Single gene reflex testing can detect these mutations, but this approach requires a variety of sample preparation methods across multiple testing platforms that can create inconsistent results. A panel approach, however, can simultaneously detect multiple mutations across these genes using one standardized sample preparation method, providing a more comprehensive and consistent approach.
This case illustrates the importance of using a robust, sensitive molecular panel approach to diagnose MPN and how different testing methods with varied levels of sensitivity may lead to inaccurate results that can negatively impact treatment decisions.

Case Work Up and Findings

- Bloodhound MPN Panel testing
- JAK2 Exon 13 mutation positive (18%)

Testing Discrepancy

Given the absence of pronounced patient symptoms, the ordering physician questioned the results, and pursued further testing for confirmation of the JAK2 Exon 13 mutation.
The patient sample was subsequently sent out to a large national reference laboratory which performed testing for JAK2 Exon 13 using an RNA-based PCR assay with a 10-15% limit of detection and reported a negative result, which contradicted the Bloodhound panel findings. However, the method used by the national reference laboratory requires more stringent sample preparation requirements due to its testing on RNA, vs Bloodhound which is tests on DNA. In addition, the 10-15% limit of detection for the second test is significantly higher than the **DNA-based Bloodhound test which has a limit of detection of 0.5% for JAK2 V617f and 2% for the other driver mutations .**
To resolve this discrepancy and ensure an accurate diagnosis, the physician ordered further confirmatory testing using Sanger sequencing, the gold standard in molecular genetic testing, albeit with a relatively higher limit of detection (10%). These tests were conducted at Precipio's clinical laboratory.

Confirmation

Sanger sequencing results confirmed the initial positive result for a JAK2 Exon 13 mutation. Both the Bloodhound MPN panel and Sanger sequencing detected the mutation at a level of roughly 18% allelic frequency, confirming the presence of the mutation, refuting the negative result from the RNA-based test found by the national reference laboratory.
Given the sample preparation differences that required parsing of the blood sample after the initial case work up and the higher (less sensitive) limit of detection, this may explain why the large national reference lab was unable to detect the JAK2 Exon 13 mutation.

The Precipio Difference:
The detection of the JAK2 Exon 13 mutation has significant clinical implications for patient treatment. The early identification of this mutation with the Bloodhound MPN Panel allowed for the initiation of hydroxyurea therapy. Hydroxyurea is a less intensive and more affordable treatment option compared to other kinase inhibitors used for advanced MPN cases.
Had the JAK2 Exon 13 mutation gone undetected, the patient would likely have progressed to a more severe stage of the disease, potentially requiring the use of more expensive, aggressive therapeutic regimens. Early treatment with hydroxyurea not only mitigates the risk of disease progression, but also improves the overall management of the patient's condition.

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