



**Patient:** John A. Doe  
**DOB/Gender:** 10/10/44 (74 yrs) - Male  
**Patient ID/MRN:** 123456  
**Date Collected:** 01/02/2023



**Case#** P23-00323  
**Status:** Final  
**Report Category:**  
**Not Detected**



**Provider:** Jane Smith, M.D.  
Hematology Oncology Associates  
Tel: 800-123-4567  
Fax: 800-765-4321

 **DIAGNOSIS:**

Peripheral blood:  
HemeScreen™ MPN results reveal:

- 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
- Negative for CALR exon 9 insertion/deletion mutations

 **INTERPRETATION**

The V617F mutation of the JAK2 (Janus kinase 2) gene has been described in polycythemia vera (PV), essential thrombocythemia (ET) and primary myelofibrosis (PMF) cases.<sup>1-2</sup> Identification of the V617F JAK2 point mutation in myeloproliferative neoplasms (MPN) is indicated in diagnosis, classification and monitoring.

Mutations in the JAK2 exon 12 & 13 (Janus kinase 2) gene are rare in ET or PMF, and their occurrence in PV is almost always associated with the absence of JAK2 V617F and the presence of a subnormal serum erythropoietin level.<sup>3</sup> The identification of the JAK2 exon 12 mutations in myeloproliferative neoplasms (MPN) may be useful to assist diagnosis, classification and monitoring. Mutations involving 13 (G571S) encoding the pseudokinase domain that regulates the tyrosine kinase activity of JAK2.

MPL (W515L/K) mutations of the juxtamembrane region of the thrombopoietin receptor MPL (myeloproliferative leukemia virus oncogene homology) have been described in JAK2 V617F-negative primary myelofibrosis (PMF) and essential thrombocythemia (ET).<sup>5</sup> The identification of W515 L/K point mutations in myeloproliferative neoplasms (MPN) may be useful to assist diagnosis, classification and monitoring.

The gene encoding calreticulin (CALR) is mutated in the majority (~70-85%) of essential thrombocythemia (ET) and primary myelofibrosis (PMF) cases with non-mutated JAK2.<sup>5,6</sup> CALR mutations have been found to be the second most frequent genetic mutation in myeloproliferative neoplasms (MPN) after Jak2.<sup>6,7</sup> Mutations in CALR have been reported to be mutually exclusive with mutations in both JAK2 and MPL and are not reported in polycythemia vera (PV).<sup>6-8</sup>

The identification of CALR Exon 9 insertion/ deletion mutations in myeloproliferative neoplasms (MPN) may be useful to assist diagnosis, classification and monitoring.<sup>6-8</sup> In addition the presence of CALR mutations has been associated with a more benign clinical course in comparison to corresponding disorders associated with JAK2 or MPL mutations.<sup>6-9</sup>

**REFERENCES:**

1. Baxter et al. The Lancet 2005: 1054 - 1061
2. Levine et al. Cancer Cell 2005: 387-397
3. Pardanani et al Leukemia 21: 2007;

4. Pietra et al Blood 111: 2008
5. Pancrazzi et al. JMD 2008: 435 - 441
6. Nangalia et al. N Engl J Med. 2013;369(25):2391-405
7. Klampfl et al. N Engl J Med. 2013;369(25):2379-90
8. Rumi et al. Blood.2013 Dec 23.
9. Rotunno et al. Blood.2013 Dec 26.

**METHOD:**

High resolution melting (HRM), produces curves using dyes that fluoresce in the presence of DNA. As the temperature increases, the fluorescence decreases as a result of the denaturation of the DNA, producing a characteristic melt profile.

This assay can detect mutations with a minimum sensitivity of 5% MAF (mutant allele frequency). Although molecular testing is highly accurate, rarely false-positive and false-negative diagnostic errors may occur.

HRM analysis was performed using ThermoFisher's HRM software v3.2

**Electronically Signed By:** Frank Bauer, MD, Precipio, Inc. (01/04/2023 11:00)



**CLINICAL DATA**

ICD-10: D75.1, D75.9. Secondary polycythemia. New diagnosis.

Received CBC, reported on 12/28/2022: WBC 7.8; RBC 5.63; HGB 17.2; HCT 53.1; MCV 94.0; MCH 30.6; MCHC 32.5; RDW 13.8%; PLT 162; MPV 7.2; LYM 12.9%; GRAN 81.9%; MID NP; MON 5.2%; NEU NP; EOS NP; BAS NP; (NP = not provided)

Disclaimer: The adequacy of staining is verified by the appropriate LSI controls. The reagents used for these assays are for research use only (RUO). Their performance characteristics have been initiated by Precipio, Inc., New Haven, CT. They have not been reviewed by the FDA. The FDA has deemed that such approval is unwarranted for clinical use. These assays should be viewed as experimental and/or research use only.



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**Received Information:** 1 green-top tube(s), 2 lavender-top tube(s)



**Received:** 01/02/2023 10:39



**Reported:** 01/04/2023 11:30