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MC-4055

To: DR. SISIR KR PATRA
-
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Kolkata- 700099
West Bengal
Report Of: MD. MUZIBAR RAHMAN

Sample ID	:	2300130396	
Patient ID	:	1002355414	
Collected on	:	14-07-2023	
Received on	:	15-07-2023 14:00:00	
Reported on	:	19-07-2023 16:27:56	
Ref By	:	DR.SISIR KR PATRA	

MOLECULAR GENETICS REPORT

Patient Name	: **MD. MUZIBAR RAHMAN**	**Age**	: **44 Years**
Physician Name	: **DR.SISIR KR PATRA**	**Gender**	: **Male**
Provisional Diagnosis	: **Chronic myeloproliferative disease**	**Specimen Status**	: **Ok**
Specimen Type	: **Bone Marrow Aspirate (BMA)**	**Disease Status**	: **At Diagnosis**
Test Requested	: **BCR-ABL1 transcript by breakpoint analysis (Qualitative analysis), JAK2 V617F, JAK2 Exon12, CALR and MPL in Myeloproliferative Neoplasms**		

Test : JAK2 V617F, JAK2 Exon12, CALR and MPL in Myeloproliferative Neoplasms Analysis.

Result: Positive

JAK2 V617F, JAK2 Exon12, CALR and MPL in Myeloproliferative Neoplasms Analysis:

Gene	Exon	Codon	Result	Mutation	COSMIC ID	Clinical significance
JAK2	14	V617	Negative	-	-	-
JAK2	12	-	Negative	-	-	-
MPL	10	W515	Negative	-	-	-
CALR	**9**	**-**	**Detected**	**c.1154_1155insTTGTC; p.K385Nfs*47**	**COSM1738056**	**Pathogenic**

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Conclusion: The specimen tested positive for one of the common 5-bp insertion (type-II mutation) in CALR exon 9. As per literature, the type-2 like CALR mutation has been preferentially associated with an essential thrombocythemia phenotype, low risk of thrombosis despite very-high platelet counts and indolent clinical course with long term survival. The specimen tested negative for JAK2 V617F mutation, JAK2 exon 12 mutations and MPL W515K/L mutation. Kindly correlate with clinical findings.

Interpretation:
Myeloproliferative neoplasms (MPN) frequently harbor the JAK2 V617F mutation in exon 14 in more than 95% of patients with Polycythemia Vera (PV), and about 60% of patients with essential thrombocytosis (ET) and primary myelofibrosis (PMF) Literature reports indicate a lower incidence of exon 12 mutations in the western population as compared to the Asian population suggesting an uneven geographic distribution. The CALR mutation frequencies in patients with ET and PMF were around 19% and 22%, respectively. The MPL mutation frequencies in patients with ET and PMF were around 6% and 10%, respectively.

Methodology:
DNA was extracted from the specimen and JAK2 V617F mutation analysis was carried out using allele-specific polymerase chain reaction which can detect both wild type and mutant allele in the presence of an internal control which is a fragment of the JAK2 sequence. The analytical sensitivity of the assay has been determined to be 5% of tumor load. DNA reference sequence is NM_001322194.1, protein reference sequence is NP_001309123.1. The MPL mutant is detected by allele-specific polymerase chain reaction which can detect the wild-type allele as well as the two mutant alleles i.e. W515L and W515K; JAK2 Exon 12 mutation and CALR mutation were detected by DNA sequencing using capillary electrophoresis of their respective coding regions. The analytical sensitivity is determined to be 15% of the tumor load. Reference sequences for MPL: NM_005373.2 & NP_005364.1; for CALR: NM_004343.3 & NP_004334.1

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References:

1. Labastida-Mercado. et al. The mutation profile of JAK2, MPL and CALR in Mexican patients with philad elphia chromosome-negative myeloproliferative neoplasms. Hematol Oncol Stem Cell Ther 2015; 8(1) : 16-21.
2. Teofili et al. Markers of Myeloproliferative Diseases in Childhood Polycythemia Vera and Essential Thr ombocythemia. J Clin Oncol.2007; 25:1048-1053.
3. Pietra D. et al. Differential clinical effects of different mutation subtypes in CALR-mutant myeloprolife rative neoplasms. Leukemia 2016;30(2):431-438.
4. Rumi E, et al. Clinical effect of driver mutations of JAK2, CALR, or MPL in primary myelofibrosis. Blood. 2014;124(7):1062-9.
5. Klampfl T, Gisslinger H, Harutyunyan AS, et al. Somatic mutations of calreticulin in myeloproliferative neoplasms. N Engl J Med. 2013;369(25):2379-2390.
6. Cazzola Maria. et al. Mutant calreticulin: when a chaperone becomes intrusive. Blood 2016;127(10):1 219-1221.
7. Tefferi A. Calreticulin mutations and long-term survival in essential thrombocythemia2014 Dec;28(12):2300-3. doi: 10.1038/leu.2014.148. Epub 2014 May 5.

Prepared By : **Mr. Rohit Waghole**
Verified By : **Dr. Aniket Prabhudesai**

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- End of Report -

Conditions of Reporting/Disclaimer:

- This report is based on the sample received in the Lilac Insights laboratory; the analysis is based on the assumption that samples received are representative of the patient mentioned on the test requisition form and the sample. When samples are received from various referral centers, it is presumed that patient demographics are verified at the point of sample collection.
- All samples for molecular studies must be collected in EDTA tubes (lavender cap). A sample where the test requisition requires RNA and subsequent cDNA conversion, must be maintained and transported at 4°C until it reaches Lilac Insights Pvt. Ltd. within 24 hours to prevent degradation of the RNA in the sample. FFPE tissue blocks often yield fragmented DNA of low concentrations which can impact result quality.
- Assays are performed in accordance with standard procedure on receipt. The reported results are dependent on individual assay methods, equipment used, method specificity, sensitivity and quality of specimen(s) received.
- Despite all the necessary precautions and stringency adopted whilst performing DNA tests, the currently available data indicates that the technical error rate associated with all types of DNA analysis, is approximately 2%.
- Although molecular testing is highly accurate, rarely false-positive & false-negative diagnostic errors may occur due to improper quality control during sample collection, cellular integrity of sample, selection of inappropriate specimen and/or presence of PCR inhibitors. PCR primer binding site polymorphisms or mutations might lead to allele dropout & cause false negative results.
- It is important that all clinicians or persons requesting DNA diagnostic tests are aware of these data before acting upon these results. As with all diagnostic tests, the laboratory report must be interpreted in conjunction with the presenting clinical profile of the patient and evaluation of all reports.
- In sequencing based tests sometimes variants of unknown significance (VUCS) are detected that have either not been reported before, and/or whose effect cannot be determined based on the current knowledge standards and reporting guidelines. In such cases, we recommend periodic review of these variants to determine any change in classification based on new published research.
- Lilac Insights Pvt. Ltd. has policy to return the FFPE blocks within one month after final reporting with proper documentation of the dispatch of the block to customer from accession dept, Lilac. After dispatch, if there is no intimation from customer within two weeks, Lilac will not be responsible for the dispatched FFPE block.
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Test : BCR-ABL1 transcript by breakpoint analysis (Qualitative analysis) Analysis.

Result: Negative

BCR-ABL1 transcript by breakpoint analysis (Qualitative analysis) Analysis:

BCR-ABL1 fusion transcript	BCR-ABL1 transcript type	ABL1 control gene
Not detected	**-**	**Detected**

Conclusion: The specimen does not show the presence of any of the BCR-ABL1 fusion transcripts, i.e., p210 transcript (b2a2 or b3a2) and p190 transcript (e1a2). Kindly correlate with clinical findings.

Note: Atypical BCR-ABL1 transcript apart from p210 and p190 can be detected by FISH.

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Methodology:
Total RNA was extracted from the specimen, reverse transcribed and the type of BCR-ABL1 transcript is determined (e1a2 or b2a2, b3a2) by qualitative polymerase chain reaction using breakpoint analysis. ABL1 serves as an endogenous reference control.

References:

1. Jones C. D., Yeung C., et al. Comprehensive validation of a real-time quantitative bcr-abl assay for cli nical laboratory use. Am J ClinPathol. 2003; 120: 42-48
2. Hu L-H, Pu L-F, Yang D-D, et al. How to detect the rare BCR-ABL (e14a3) transcript: A case report and literature review. Oncology Letters. 2017;14(5):5619-5623. doi:10.3892/ol.2017.6847.

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