hema CŌRE

BCR-ABL1 KD Gene Sequencing

Specimen Type	
EDTA PERIPHERAL BLOOD	
Specimen Collection Date & Time	Date & Time of Accessioning
27/05/2024	29/05/2024 11:24 Hrs

Case Number:	**102240085870**
Patient Name:	**AMINATH NASHIDA**
Age/Sex:	**43 Yrs/Female**
Patient Location:	**Colombo**
Hospital Name:	**Aegle Omics (Private) Limited**
Physician Name:	**Dr. Mahendra Perera**
Date & Time of Reporting:	**15/06/2024 18:23 Hrs**

TEST METHODOLGY

Total Blood RNA was isolated from Peripheral Blood is used for NGS Library preparation.
The libraries were sequenced to mean depth: >1000xon next generation sequencing platform.
The raw read sequences obtained from NGS are processed to remove adapters and filter poor quality reads.
Clinically relevantmutations were identified and annotated using published variants in literature and a set of diseases databases.

CLINICAL HISTORY

Chronic pain

RESULTS SUMMARY

- **IRMA: Negative**

Gene & Transcript	Variant	Depth	Mutant Allele%	Clinical Significance	Sensitivity to Imatinib
None					

CLINICAL SIGNIFICANCE

- Chronic myelogenous leukemia (CML) is characterized by the presence of the Philadelphia chromosome, the product of the t (9;22)(q34;q11) translocation. This translocation results in the BCR/ABL fusion protein with constitutive ABL tyrosine kinase activity.
- CML accounts for approx20% of all adult leukaemias. Imatinib is a targeted tyrosine kinase inhibitor for patients suffering from Chronic Myeloid Leukemia (CML). Patients' response to Imatinib has been significantly better and with fewer side effects than other available therapies.
- The kinase inhibitor imatinib inhibits ABL kinase activity and is now the standard of care for early phase CML. Prolonged treatment with imatinib can lead to drug resistance, especially in patients with advanced disease.

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- A large portion of resistant patients have acquired point mutations in the ABL kinase domain that renders the kinase resistant to the drug. Sites of point mutations in ABL associated with imatinib resistance span the entire kinase domain but often cluster in important hotspots.
- Patients who initially responded well to Imatinib have at times relapsed due to the development of resistance caused by changes in the ABL1 kinase domain. This affects Imatinib's ability of binding to the active site. CML patients on Imatinib are monitored with quantitative RT-PCR and that patients with a log increase in quantitative BCR-ABL1 transcript levels are recommended to be assayed for the presence of Imatinibresistance mutations.
- This Next generation sequencing test interrogates mutations in ABL1 kinase domain. Next Generation sequencing based IRMA screening can offer early resistance analysis as NGS allows detection of >1% allele fraction detection. Traditional sanger sequencing requires atleast 20% allele fraction for detection of mutation.
- Upon understanding the mutation status, the clinician intervenes by increasing the dosage of Imatinib or Switching to second generation inhibitors or Alternate treatment options depending on the exact mutation present that may be effective in controlling BCR -ABL1 levels.

RECOMMENDATIONS

- We recommend confirming the presence variants by Sanger Sequencing.
- The results should be interpreted in the context of the patient's medical evaluation. Correlation of the genetic findings with the clinical condition of the patient is required to arrive at accurate diagnosis, prognosis or for therapeutic decisions.

REFERENCES

1. Soverini, Simona, et al. "Bcr-Abl kinase domain mutation analysis in chronic myeloid leukemia patients treatedwith tyrosine kinase inihibitors: recommendations from an expert panel on behalf of European LeukemiaNet." Blood (2011): blood-2010.
2. Gorre, Mercedes E., et al. "Clinical resistance to STI-571 cancer therapy caused by BCR-ABL gene mutationor amplification." Science 293.5531 (2001): 876-880

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Question?

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This is a transcribed report and the test was performed at the laboratory OSL 14.