PRECIPIO EXPECT MORE.
203-787-1717
203-901-1289

MOLECULAR

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:
Detected

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

DIAGNOSIS:

Bone marrow, aspirate:
HemeScreen™ CLL results reveal:
- Negative for CXCR4 mutation
- Positive for MYD88 mutation* see comment
- Negative for NOTCH1 mutation
- Negative for SF3B1 mutation

COMMENT

MYD88 exon 5 variant detected. Base change c.794T>C. Protein change p.L265P.

INTERPRETATION

CXCR4 receptor protein activates signaling pathways for proliferation, cell growth and differentiation. CXCR4 overexpression is associated with more aggressive disease. Studies show an increase in migratory potential in those with high levels of CXCR4. (4, 5)

MYD88 codes for a protein involved in signaling within immune cells. MYD88 mutation is often related with IgVH-mutation and has shown no significant impact on overall survival. MYD88 mutation is exclusive of NOTCH1 and SF3B1. MYD88 mutation appears less frequently when CD38 is greater than or equal to 30%. (1, 6)

NOTCH1 (Notch Homolog 1) is considered an oncogene and a tumor suppressor due to the diverse function. Poor prognosis, shorter treatment-free survival and <10 yr overall survival is commonly seen in NOTCH1 mutated CLL. NOTCH1 mutation is seen with unmutated IgVH, deletion 13q14, deletion 17p and trisomy 12. Individuals with NOTCH1 mutated CLL have a higher incidence of Richter's syndrome. NOTCH1 mutation is often correlated with CD38 being greater than or equal to 30%. (1, 2, 3, 6)

SF3B1 (Splicing Factor 3b Subunit 1) is involved in DNA repair; mutation of this gene causes dysregulation of the maintenance of DNA. SF3B1 mutation is commonly associated with unmutated IgVH, fludarabine-resistance, and concurrent TP53 mutation. This mutation is associated with poor outcome, <10 yr survival. Studies have shown SF3B1 mutation are later events in diseases progression. (1, 2, 7)

REFERENCES:

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5. Ganghammer S, Gutjahr J, Hutterer E, et al. Combined CXCR3/CXCR4 measurements are of high prognostic value in chronic lymphocytic leukemia due to negative co-operativity of the receptors. Haematologica. 2016;101(3):e99-e102. doi:10.3324/haematol.2015.133470
6. Xia Y, Fan L, Wang L, et al. Frequencies of SF3B1, NOTCH1, MYD88, BIRC3 and IGHV mutations and TP53 disruptions in Chinese with chronic lymphocytic leukemia: disparities with Europeans. Oncotarget. 2015;6(7):5426-5434. doi:10.18632/oncotarget.3101
7. Youzhong Wan, Catherine J. Wu; SF3B1 mutations in chronic lymphocytic leukemia. Blood 2013; 121 (23): 4627-4634. doi: https://doi.org/10.1182/blood-2013-02-427641

METHOD

Melting curve analysis in combination with real-time PCR is a natural extension of continuously monitored PCR within each cycle. During high resolution DNA melting analysis (HRM or HRMA), melting curves are produced using dyes that fluoresce in the presence of double-stranded DNA (dsDNA). Using specialized instruments designed to monitor fluorescence during heating; as the temperature increases, the fluorescence decreases, producing a characteristic melting profile.

This assay can detect mutations with a minimum sensitivity of 2% depending on the wild type background in the specimen. Although molecular testing is highly accurate rarely false-positive and false-negative diagnostic errors may occur.

HRM analysis was performed using HRM v3.1 Thermo Fisher software to discriminate DNA sequences based on their composition, length, GC content, or strand complementarities.

Electronically Signed By: Frank Bauer, MD, Precipio, Inc. (01/06/2023 11:00)

CLINICAL DATA

ICD-10: D47.2, D61.818, N18.31, Z13.79, D75.9, C85.80. Pancytopenia. Monoclonal gammopathy. Chronic kidney disease, stage 3a. New diagnosis.

Received CBC, reported on 12/30/2022: WBC 4.2; RBC 2.71; HGB 8.6; HCT 26.3; MCV 97.1; MCH 31.6; MCHC 32.6; RDW 14.6%; PLT 119; MPV 7.2; LYM 41.3%; GRAN 51.4%; MID NP; MON 7.3%; 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.

The reagents used for these assays are for research use only (RUO). Confirmatory sanger sequencing performed by Precipio, Inc. in its location in Omaha, NE (CLIA#: 28D2215036). The reagents have not been reviewed by the FDA. The assays should be viewed as experimental and/or research use only.

Patient: John A. Doe
Case #: P23-00323
Received Information: 1 lavender-top tube(s)
Received: 01/03/2023 10:30
Reported: 01/06/2023 12:30