PacificDx

FibroSIGHT™ Plus

Patient name Monfort, Gary
DOB 1 Jan 1970
Accession ID CLNFS-001

PATIENT		PHYSICIAN	
Name:	Monfort, Gary	**Ordering Physician:**	Dr ABC, MD
DOB:	1 Jan 1970	**Account Number:**	N/A
MRN:	XYZ6789123	**Practice/ Facility:**	Liver Health Medical Centre
Sex:	Male	**Report copied to:**	N/A
		Pathologist:	Dr XYZ Pathology Labs

SPECIMEN DETAILS

Accession ID:	CLNFS-001	**Report Date:**	01/09/2025	**Specimen ID:**	SP24-0000
Receipt Date:	12/23/2024	**Specimen Type:**	Unstained FFPE slides	**Biopsy Date:**	11/07/2024

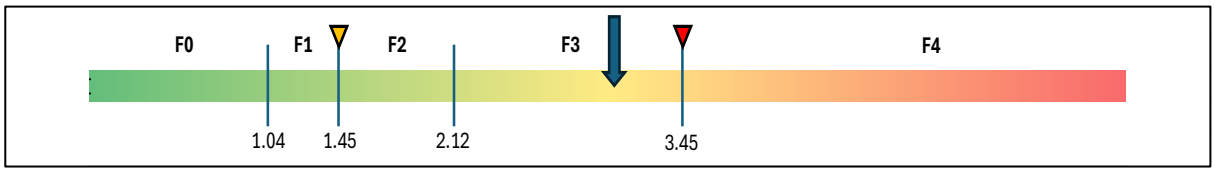
CLINICAL INFORMATION	TREATMENT INFORMATION
Abnormal liver enzymes, percutaneous liver biopsy.	None

RESULTS

Fibrosis Assessment: FibroSIGHT™ Plus

qFibrosis Value	**3.05**
Classification	**At-risk MASH**

This specimen shows a qFibrosis value of 3.05, which corresponds to NASH-CRN fibrosis stage 3. This is consistent with at-risk MASH.



The colorbar image above shows the pre-determined cut-offs for NASH-CRN fibrosis stage classification according to qFibrosis value. The blue vertical arrow indicates where the current specimen's score falls on the scale of qFibrosis values. Specimen with qFibrosis value less than 1.45 (▼) corresponds to not at-risk MASH; specimen with qFibrosis value of more than or equal to 1.45 (▼) corresponds to at-risk MASH; specimen with qFibrosis value of more than 3.45 (▼) corresponds to cirrhotic MASH.

Prescription information for Rezdiffra (FDA, 2024).

TEST METHODOLOGY

FibroSIGHT™ Plus is a proprietary digital pathology assessment tool developed by HistoIndex Pte. Ltd and designed for automated evaluation of fibrosis of MASH liver biopsies. FibroSIGHT™ Plus quantifies fibrosis-related collagen features through analysis of images generated from HistoIndex's Second Harmonic Generation (SHG) microscopy platform, which enables high-resolution and consistent visualization of fibrillar collagen and pathological fibrosis in unstained FFPE liver biopsy sections (Sun, et al., 2008). Selected features that have been determined to be highly correlated to NASH-CRN fibrosis stages, are then incorporated into a proprietary linear regression model - qFibrosis® - to generate a numerical index on a continuous scale (qFibrosis value) corresponding to the extent of fibrosis in the biopsy sample. The qFibrosis value is then translated into ordinal stages corresponding to NASH-CRN fibrosis stages (Kleiner, et al., 2005), using pre-determined cut-offs that maximize the performance of the qFibrosis model in predicting NASH-CRN stages. For a given sample, qFibrosis values and stages are calculated in a fully automated manner from SHG images of MASH liver biopsies.

During development and internal validation of qFibrosis model, Spearman's correlation coefficient of association of predicted qFibrosis values and NASH-CRN fibrosis stages was 0.816 ($p<0.0001$), and in an independent external validation cohort (Kendall, et al., 2024), the Spearman's correlation coefficient was 0.74 ($p<0.0001$) indicating consistent predictive accuracy on a continuous scale. In another validation study of 120 MASH biopsies with consensus fibrosis stages assigned by a panel of expert pathologists as reference, automated fibrosis stage readouts obtained from FibroSIGHT™ Plus' qFibrosis showed higher concordance with the reference compared to Masson's Trichrome-stain-based stages assigned by community pathologists, with a Spearman's correlation coefficient of 0.81 ($p<0.0001$) for qFibrosis values.

LIMITATIONS AND DISCLAIMERS

FibroSIGHT™ Plus test is regulated under the Clinical Laboratory Improvement Amendments (CLIA) of 1988 for high-complexity testing. This test has not been approved by the U.S. Food and Drug Administration (FDA). The FibroSIGHT™ Plus test performance characteristics were determined by PacificDx.. The test is intended to assist clinicians in making patient management decisions and should be interpreted alongside other clinical data and relevant treatment guidelines. This test is conducted for clinical purposes only and should not be considered investigational or for research. Clinical validation has been established only for unstained FFPE liver biopsy sections of patients with metabolic-dysfunction associated steatohepatitis (MASH). This test is performed by PacificDx.

REFERENCES

Kendall, T., Chng, E., Ren, Y., Tai, D., Ho, G., & Fallowfield, J. (2024). Outcome prediction in metabolic dysfunction-associated steatotic liver disease using stain-free digital pathological assessment. Liver International, 2511-2516.

Kleiner, D. E., Brunt, E., Van Natta, M., Behling, C., Contos, M., Cummings, O., . . . Yeh, M. (2005). Design and validation of a histological scoring system for nonalcoholic fatty liver disease. Hepatology, 1313-1321.

Sun, W., Chang, S., Tai, D., Tan, N., Xiao, G., Tang, H., & Yu, H. (2008). Nonlinear optical microscopy: use of second harmonic generation and two-photon microscopy for automated quantitative liver fibrosis studies. Journal of biomedical optics, pp.064010-064010.

U.S. Food and Drug Administration (FDA). (2024). REZDIFFRA: HIGHLIGHTS OF PRESCRIBING INFORMATION. REZDIFFRA is a thyroid hormone receptor-beta (THR-beta) agonist indicated in conjunction with diet and exercise for the treatment of adults with noncirrhotic nonalcoholic steatohepatitis(NASH) with moderate to advanced liver fibrosis (consistent with stage F2 to F3 fibrosis). https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/217785s000lbl.pdf