
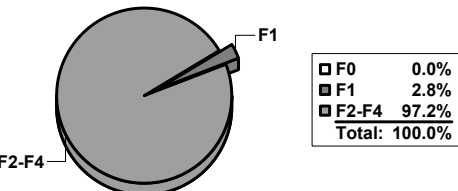


Added clarity in detecting liver fibrosis

 PROMETHEUS® Therapeutics & Diagnostics 9410 Carroll Park Drive San Diego CA 92121 Toll Free: 888/423-5227 www.prometheuslabs.com		Test Results SAMPLE REPORT PROMETHEUS® FIBROSpect II	
Patient & Order Information Order ID: 2081520 Patient: Test, Patient DOB: 01/01/1950 SSN: XXX-XX-6789 Sex: X Institution ID: XXXXX Prometheus ID: 1406851 Ordered: 01/03/2011 Completed: 01/04/2011 Ordered By: Undefined Physician MD ICD9 Codes: 276.8 787.03 Sample ID: SM01030080 Collection Date: 12/29/2010 5:00AM (Serum)		Report Recipient Undefined Physician MD Prometheus Laboratories Inc. 9410 Carroll Park Drive San Diego, CA 92121 858/824-0895 Phone 858/824-0896 Fax Institution Sample ID: RE2R	
Test Result			
1. FIBROSpect II Index 99	2. Clinical Interpretation Consistent with METAVIR F2-F4	3. FIBROSpect II Index Reference Range 0 - 41 Consistent with METAVIR F0-F1 42 - 100 Consistent with METAVIR F2-F4	
1. FIBROSpect II Index Interpretation In a study population of chronic HCV patients (n=696), 0.3% of patients with biopsy F0-F1 had a FIBROSpect II index of >= 99. Of these, 0.0% were F0 and 100.0% were F1.		2. FIBROSpect II Index >= 99 (N= 36) 	
2. Clinical Interpretation Based on this study population and these results, the chance of your patient having F2-F4 is 97.2%.* The chance of having F0 is 0.0% and the chance of having F1 is 2.8%.		3. METAVIR Description (1,2): F0 - No fibrosis F1 - Portal tract fibrosis F2 - Septal fibrosis F3 - Bridging fibrosis F4 - Cirrhosis	
3. Reference Range Studies In a study population of chronic HCV patients (n=696) with a fibrosis (METAVIR F2-F4) prevalence of 51.7%, FIBROSpect II sensitivity at an index of 42 was 81% and the specificity was 71%. Tests performed to determine FIBROSpect II result: a2-macroglobulin (AMG) by nephelometry, Tissue inhibitor of metalloproteinases-1 (TIMP-1) by ELISA, Hyaluronic acid (HA) by ELISA. This test was developed and its performance characteristics determined by Prometheus Laboratories Inc. It has not been cleared or approved by the U.S. Food and Drug Administration.			
1) French METAVIR Cooperative Study Group. Intraobserver and interobserver variations in liver biopsies in patients with chronic hepatitis C. <i>Hepatology</i> 1994;20:15-20. 2) Elizabeth M. Brunt, Hepatology at the millenium grading and staging the histopathological lesions of chronic hepatitis: The Knodell histology activity index and beyond, <i>Hepatology</i> 2000;31:241-246.			
Notes: Prometheus diagnostic services provide important information to aid in the diagnosis and management of certain diseases. Test results should be used with other clinical and diagnostic findings to make a diagnosis and prognosis. This test may be covered by one or more US pending or issued patents - see prometheuslabs.com for details.			
Curtis A. McGuyer MD Medical Director		Prometheus, the Link Design, and FIBROSpect II are registered trademarks of Prometheus Laboratories Inc.	
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References: 1. Wong VS, Hughes V, Trull A, et al. Serum hyaluronic acid is a useful marker of liver fibrosis in chronic hepatitis C virus infection. *J Viral Hepat.* 1998;5(3):187-192. 2. Boeker KH, Haberkorn CI, Michels D, et al. Diagnostic potential of circulating TIMP-1 and MMP-2 as markers of liver fibrosis in patients with chronic hepatitis C. *Clin Chim Acta.* 2002;316(1-2):71-81. 3. Poynard T, Ratziv V, Benmanov Y, et al. Fibrosis in patients with chronic hepatitis C: detection and significance. *Semin Liver Dis.* 2000;20(1):47-55. 4. METAVIR Cooperative Study Group. Intraobserver and interobserver variations in liver biopsy interpretation in patients with chronic hepatitis C. *Hepatology.* 1994;20(1 Pt 1):15-20. 5. Patel K, Benhamou Y, Yoshida EM, et al. An independent and prospective comparison of two commercial fibrosis marker panels (HCV FibroSURE and FIBROSpect II) during albuterferon alfa-2b combination therapy for chronic hepatitis C. *J Viral Hepat.* 2009;16(3):178-186. 6. Patel K, Nelson DR, Rockey DC, et al. Correlation of FIBROSpect II with histologic and morphometric evaluation of liver fibrosis in chronic hepatitis C. *Clin Gastroenterol Hepatol.* 2008;6(2):242-247. 7. Zaman A, Rosen HR, Ingram K, et al. Assessment of FIBROSpect II to detect hepatic fibrosis in chronic hepatitis C patients. *Am J Med.* 2007;120(3):280.e9-14. 8. Christensen C, Bruden D, Livingston S, et al. Diagnostic accuracy of a fibrosis serum panel (FIBROSpect II) compared with Knodell and Ishak liver biopsy scores in chronic hepatitis C patients. *J Viral Hepat.* 2006; 13(10):652-658.



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PROMETHEUS®
FIBROSpect II

Noninvasive testing for liver fibrosis



Added diagnostic options

PROMETHEUS® FIBROspect® II — noninvasive serodiagnostic technology may reduce the need for liver biopsy

- Aids in evaluating liver fibrosis without biopsy-associated limitations, including:^{1,2,3}
 - Sampling error
 - Interpretation subjectivity
 - Morbidity and mortality
 - Patient discomfort and cost
- May be repeated more frequently, easily and safely than biopsy
- May be useful as an adjunct to biopsy or when biopsy is contraindicated
 - Patients with clotting factor problems, prior biopsy, biopsy refusal and relapse/nonresponse to HCV treatment
- Assists in treatment decisions for patients with hepatitis C

The use of only extracellular matrix (ECM) markers distinguish PROMETHEUS FIBROspect II from other serodiagnostic tests

- Unique set of markers combined with a proprietary algorithm to help diagnose liver fibrosis
 - **Tissue inhibitor of metalloproteinase-1:** associated with ECM breakdown
 - **Hyaluronic Acid:** associated with ECM development
 - **Alpha2 Macroglobulin:** inhibits a wide spectrum of proteins which regulate ECM development

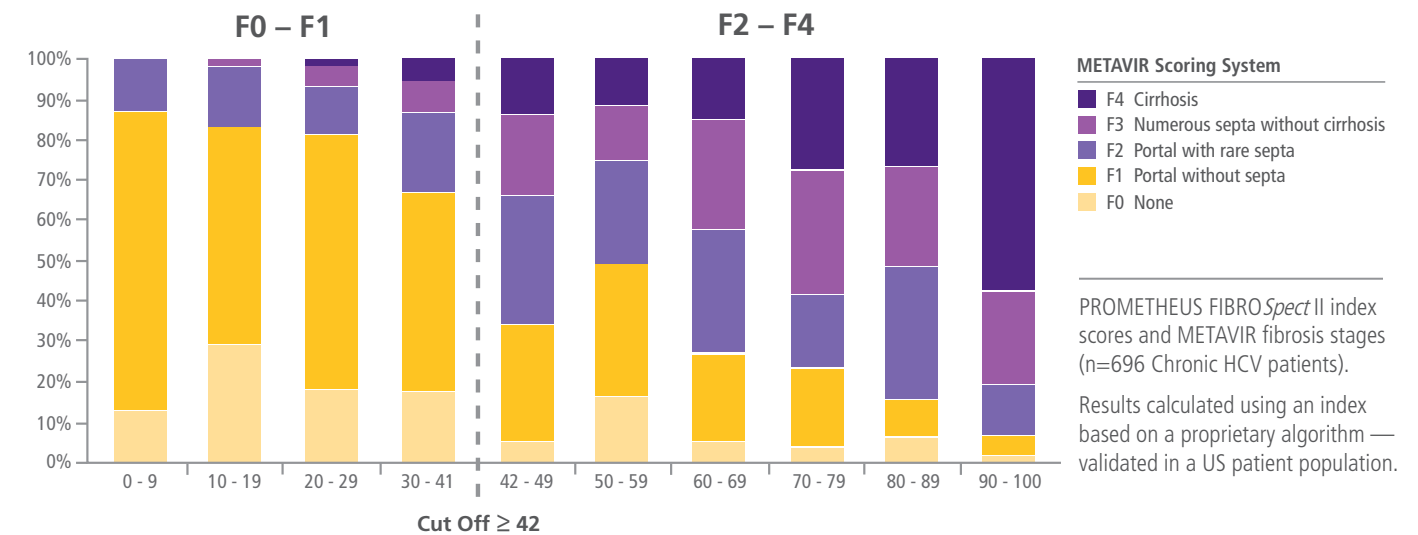
PROMETHEUS®
FIBROspect® II

Personalized performance index

PROMETHEUS FIBROspect II performance index

- Designed to differentiate no/mild liver fibrosis (METAVIR F0-F1) from significant liver fibrosis (METAVIR F2-F4)⁴
- Provides individualized test interpretation for increased confidence in test results
- No indeterminate test results

Differentiates METAVIR F0-F1 from METAVIR F2-F4 including PROMETHEUS FIBROspect II index to individualize patient results⁴



PROMETHEUS FIBROspect II has been validated by multiple peer-reviewed published studies

Performance characteristics

Patel K, et al. *J Viral Hepat.* 2009;16(3):178-186^{*,5}
Sensitivity 95%, Specificity 66%, Accuracy 90%

Patel K, et al. *Clin Gastroenterol Hepatol.* 2008;6(2):242-247^{†,6}
Sensitivity 83.5%, Specificity 66.7%, Accuracy 80.2%

Zaman A, et al. *Am J Med.* 2007;120(3):280.e9-14^{‡,7}
Sensitivity 71.8%, Specificity 74%, Accuracy 73.1%

Christensen C, et al. *J Viral Hepat.* 2006; 13(10):652-658.^{§,8}
Sensitivity 93%, Specificity 66%, Accuracy 76%

Sensitivity
Up to **95%**⁵⁻⁸

Specificity
Up to **74%**⁵⁻⁸

Accuracy
Up to **90%**⁵⁻⁸

*A 48-week, phase 2B study of chronic HCV patients (n=95) (METAVIR F0-F1 or F2-F4).
†Prospective study of chronic HCV patients (n=106) (METAVIR F2-F4).

‡Prospective study of HCV patients (n=108) (METAVIR F0-F1 or F2-F4).
§Retrospective study of HCV patients (n=142) (METAVIR F0-F1 or F2-F4).