PRO-C3 determined active fibrogenesis is a predictor of liver-related outcomes in patients with chronic hepatitis C

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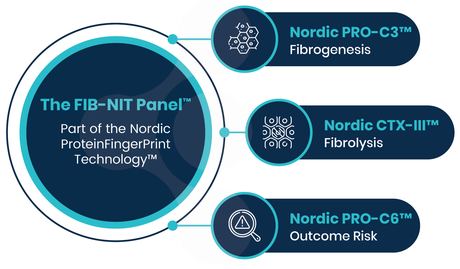
BACKGROUND

Patients with untreated chronic hepatitis C (CHC) infection are at increased risk of developing a liver-related outcome. Despite the availability of simplified direct-acting antiviral therapy, the prevalence of CHC remains unchanged in many industrialized countries. Biomarkers that can predict which chronic liver disease patients with inflammatory injury are at greatest risk of developing a clinical outcome are required.

Aim: Investigate the ability of PRO-C3 as a marker of active fibrogenesis to predict liver-related outcomes compared to METAVIR fibrosis stage on biopsy in patients with hepatitis C virus (HCV) who were non-responders to prior interferon-based standard-of-care.

METHODS

- Study population from The Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis Trial (HALT-C) including 340 patients
- Data provided by NIDDK CR, a program of the National Institute of Diabetes and Digestive and Kidney disease
- The fibrogenesis marker, NordicPRO-C3™ from The FIB-NIT Panel™, was measured in serum samples using a competitive ELISA
- METAVIR stage was assessed by liver biopsy at baseline and end-of-study



DEMOGRAPHICS

	No outcome (n=273)	Outcome (n=67)	p-value
Age (years)	51 (47.0-55.0)	50 (46.5-54.0)	0.34
BMI (kg/m²)	29.2 (26.2-32.5)	30.1 (27.2-33.1)	0.29
Sex, female	85 (31.1%)	25 (37.3%)	0.41
ALT (U/L)	89 (61-129)	84 (67-125)	0.82
PRO-C3 (ng/mL)	35.6 (26.1-54.9)	60.3 (39.5-76.7)	**p<0.0001**

Patient demographics at baseline. The table shows differences between patients who do not get an outcome and patients who do get an outcome over a median follow-up of 839 days (IQR: 474-1132). Data presented as median (IQR). BMI: body mass index, ALT: alanine aminotransferase. Outcome definitions: death, HCC, CTP≥7, variceal hemorrhage, ascites, bacterial peritonitis, and encephalopathy. p-values: Mann-Whitney U test.

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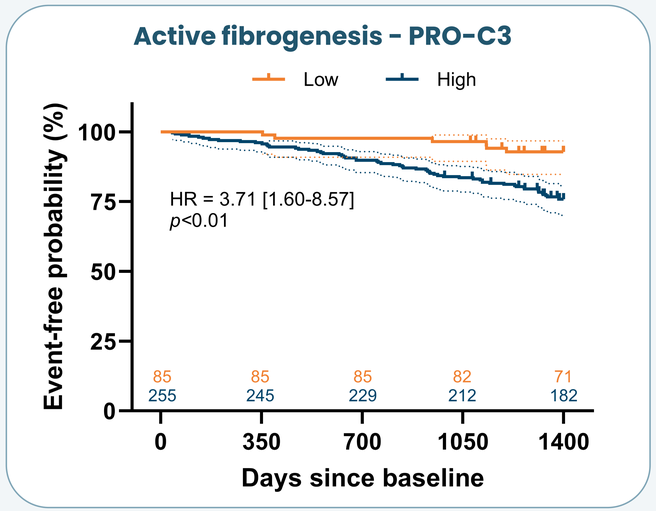
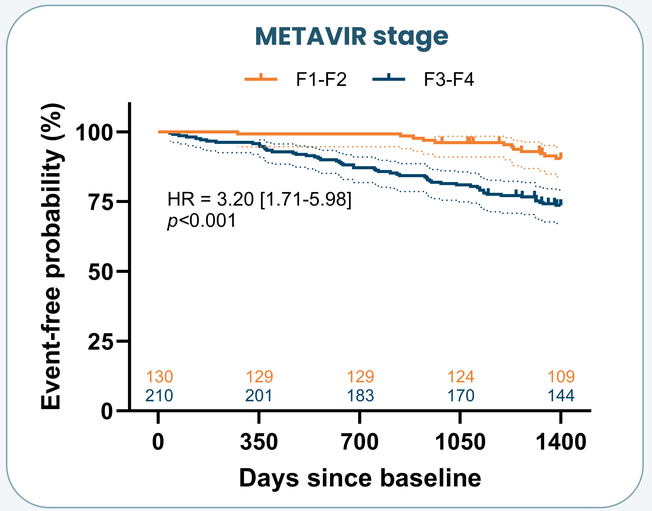
Disclosures: ES, TW, MK, and DJL are employed at Nordic Bioscience and may be shareholders
ClinicalTrials.gov identifier: #NCT00006164

RESULTS





Kaplan-Meier analysis was used to examine the event-free survival probability when stratifying into low (below Q1 in the study population, PRO-C3<27.6 ng/mL) and high (above Q1, PRO-C3>27.6 ng/mL) PRO-C3 levels or METAVIR stage (F1-F2 and F3-F4). Cox proportional hazard regression analysis (HR: hazard ratio, [95% CI]) was used to investigate the association between baseline PRO-C3 levels or METAVIR stage and the risk of a liver-related outcome.

The HR of liver-related outcomes was 3.71 times higher among patients with high baseline PRO-C3 levels compared to patients with low PRO-C3 levels

The HR of liver-related outcomes was 3.20 times higher among patients with METAVIR stage F3-F4 compared to F1-F2

KEY TAKE-HOME MESSAGES

- Fibrosis activity (PRO-C3) is associated with an increased risk of developing a liver-related outcome in patients with untreated HCV infection
- PRO-C3 provides a higher risk predictor for outcomes than METAVIR fibrosis stage on biopsy
- Pro-fibrogenic markers such as PRO-C3 could provide prognostic utility in other chronic liver disease patients with ongoing inflammatory injury

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