New non-invasive diagnostic tools dedicated to the identification of NASH patients at risk of liver outcomes are needed. We defined the regulatory agencies for the development of new NASH drugs (FDA and EMA) and the patient profile at risk as two criteria that should be pharmacologically treated.

Based on these characteristics of the patients to be treated and using the GOLDEN-505 cohort, we recently reported a diagnostic algorithm including the cirrhotic phenotype, NASH staging score, plasma levels of CHI3L1, and Hyaluronan (JHEP, 2016, vol. 64, S717).

Among the emerging biomarkers for chronic liver diseases, Chitinase-3-like protein 1 (CHI3L1, also known as YKL-40), a secreted glycoprotein. Elevated serum YKL-40 levels have been proposed as a marker of active liver disease (J Hepatol, 2004, Vol. 41, S26).

The aims of this study were:

- To compare the diagnostic performance of CHI3L1 to that of other individual variables in the identification of NASH patients to be treated.
- To assess the diagnostic performance of a new CHI3L1 including algorithm in comparison with our previous algorithm and other scoring systems.

**METHODS**

**PATIENTS AND DATA SET**

- Data set and plasma samples from the 27,000 biopsy proven NASH patients included in the GOLDEN-505 cohort were used to identify CHI3L1.
- This cohort included a wide spectrum of NASH disease activity (NAS=1-6) and severity.
- Cirrhotic patients (NAS >6) were excluded.
- Initial dataset at inclusion included more than 100 variables.

**BIOSTATISTICAL APPROACHES AND ALGORITHMS**

- Two independent biostatistical approaches (Median and Bootstrap) were used to generate diagnostic algorithms, each including patients Toot-To-Treated (TBT) from patients not-to-be-treated (NTBT).
- In both approaches, a stepwise logistic regression model was used to generate the most discriminating algorithm in the dataset and to select subsets.

**ROC ANALYSIS**

- Diagnostic performance of plasma level of CHI3L1 to discriminate Toot-To-Treated (TBT) and Not-To-Treated Patients (NTBT) were compared.
- Algorithms with and without CHI3L1 obtained by different selection approaches were also compared to discriminate TBT and NTBT through ROC analysis.

**DISCRIMINATING INDIVIDUAL VARIABLES IN GOLDEN-505**

- Additional variables:
  - Fibrosis score
  - Biopsy scoring (centralized reading):
    - Necroinflammation
    - Steatosis
  - Glucose metabolism: FPG, Insulin, HOMA-IR, Hb1AC, FFA, fructosamine
  - Liver enzymes: ALT, AST, GGT, Alkaline Phosphatase (ALK)
  - Classical biochemistry/hematology:
    - Platelets
  - HCV RNA

**REVISED ALGORITHM WITH CHI3L1**

- The most powerful algorithm has been obtained from the complete dataset and/or selected subsets.
- The inclusion of circulating levels of CHI3L1 in both the Median and the Bootstrap algorithms has been demonstrated.
- The inclusion of circulating levels of CHI3L1 in both the Median and the Bootstrap algorithms has been demonstrated.

**RESULTS**

- Compared to other previously reported algorithms, our median and bootstrap algorithms with and without CHI3L1 have higher diagnostic performance for discriminating TBT and NTBT in GOLDEN-505 cohort.
- CHI3L1 including algorithm has slightly higher diagnostic performance than other previously reported algorithms.

**CONCLUSION**

- This study demonstrates that individually plasma CHI3L1 as a diagnostic value to identify patients who should be treated in the GOLDEN-505 cohort.
- The inclusion of circulating levels of CHI3L1 in both the Median and the Bootstrap algorithms slightly, but not significantly enhances the diagnostic performances of our previously described algorithms.

**REFERENCES**