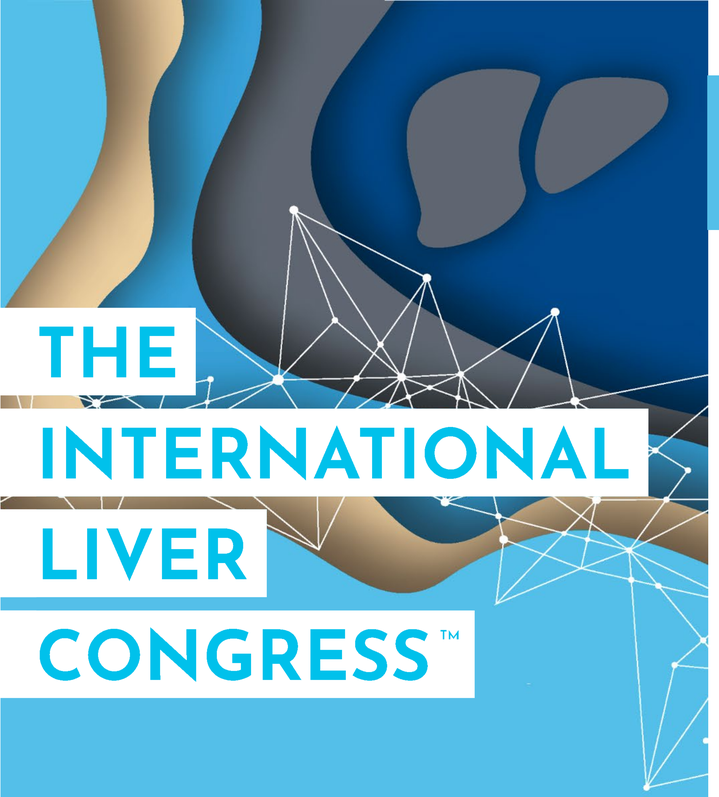

Comparative diagnostic accuracy of blood-based biomarkers for diagnosing NASH: phase 1 results of the LITMUS project

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1 Introduction

The presence of active steatohepatitis (NASH) is a regulatory requirement for NAFLD trial recruitment and an important severity indicator in clinical care. There is a pressing need for robust, non-invasive tests (NITs) to discriminate simple steatosis from NASH, but most evaluations have been non-comparative and performed in small groups.(1,2)

2 Aim

The LITMUS project independently assessed NITs that, singly or in combination, would enable detection of NASH.

3 Method

- Thirteen NITs, were evaluated against histology to identify NASH (NAS ≥ 4 with ≥1 point in each component).
- The area under the receiver operating curve (AUC) ± 95% confidence interval (95% CI) were calculated for each NIT.
- Due to the absence of any existing validated NIT for NASH and the high collinearity between NASH and fibrosis stage, FIB-4, a widely used simple fibrosis test, was adopted as a comparator in the same subgroup of patients for whom biomarker results were available.

4 Results

- Data from 720 participants from nine European centers were included.
- Mean age 50 years; 57% male; 36% type2 diabetics; mean BMI 35. Histological evidence of NASH was present in 53%.
- AUCs ranged from 0.51 to 0.78, with some marker combinations showing higher AUCs than single markers (Table 1).
- The SomaScan™ algorithm showed the highest AUC (0.78) followed by ADAPT (0.68), better than FIB-4 ($p<0.05$).

Table 1: Diagnostic accuracy of markers in detecting active NASH vs. FIB-4

NIT	n	AUC (95% CI)	
		NIT	FIB-4
CK-18 (M30)	593	0.66 (0.62-0.71)	0.62 (0.57-0.66)
CK-18 (M65)	612	0.65 (0.61-0.70)	0.61 (0.57-0.66)
PRO-C3	444	0.64 (0.59-0.69)	0.62 (0.57-0.68)
PRO-C4	391	0.62 (0.54-0.69)	0.61 (0.54-0.68)
ADAPT	444	0.68 (0.63-0.73)	0.62 (0.57-0.68)
FIBC3	440	0.65 (0.59-0.70)	0.63 (0.58-0.68)
ABC3D	440	0.64 (0.59-0.70)	0.63 (0.58-0.68)
DIAFIR	288	0.66 (0.58-0.74)	0.60 (0.53-0.67)
MACK-3	400	0.65 (0.59-0.70)	0.59 (0.53-0.65)
GLP (fibrosis)	323	0.51 (0.44-0.57)	0.57 (0.51-0.64)
SomaScan	267	0.78 (0.73-0.84)	0.61 (0.55-0.68)
ELF	695	0.62 (0.57-0.66)	0.59 (0.55-0.63)
NFS	695	0.57 (0.53-0.62)	0.59 (0.55-0.63)

5 Conclusions

Fibrosis targeted biomarkers and single biomarkers showed limited performance in detecting NASH. However, combinations produced more promising results. Among these, the SomaScan algorithm, a novel proteomics panel specifically developed to detect NASH, and ADAPT significantly outperformed FIB-4. Validation in an expanded cohort is underway

6 Acknowledgements

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