sequential NIT algorithms to minimize the requirement for biopsy and improve accuracy overuse of single tests.

Methods The STELLAR studies (NCT03053050, NCT03053063) enrolled NASH patients with bridging fibrosis (F3) or compensated cirrhosis (F4). Baseline liver biopsies were read using the NASH CRN fibrosis classification and noninvasive fibrosis markers: FIB-4 index, ELF test, and FibroScan® (FS). The performance of these tests to discriminate advanced fibrosis was evaluated using AUROCs with 5-fold cross-validation repeated 100x. Thresholds were obtained by maximizing specificity given $\geq 85\%$ sensitivity. The cohort was divided (80%/20%) into evaluation/validation sets. The evaluation set was further stratified 250x into training and test sets (66%/33%). Optimal thresholds were derived as the average across training sets, and applied sequentially (FIB-4 followed by ELF and/or FS) to the validation set. Data are from an interim analysis on 26 July 2018.

Results All patients with available liver histology (N=3202, 71% F3-F4) and NIT results were included. While single tests were able to discriminate advanced fibrosis (AUROCs of 0.78, 0.80, and 0.80 for FIB-4, ELF, and FS in validation cohort), up to 32% of patients had an indeterminate result. Using thresholds derived from STELLAR data, FIB-4 followed by FS or ELF in those with indeterminate FIB-4 values (1.23 to 2.1) reduced indeterminate results to as low as 13% (table 1). Published NIT thresholds yielded similar results (data not shown). Adding a third test (FIB-4 then ELF then FS) reduced the rate of indeterminate results to 8%. Misclassification occurred at rates similar to biopsy (15–21%). The majority of misclassifications (63–81%) were false negatives; among false positive cases (19–27% of misclassifications) up to 70% had F2 fibrosis.

Conclusions FIB-4 followed by ELF and/or FS nearly eliminated the need for liver biopsy and accurately identified patients with advanced fibrosis due to NASH with misclassification rates similar to liver biopsy.

IDDF2019-ABS-0133

ROUTINELY AVAILABLE NONINVASIVE TESTS DISCRIMINATE ADVANCED FIBROSIS DUE TO NASH IN THE PHASE 3 STELLAR TRIALS OF THE ASK1 INHIBITOR SELONSERTIB

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10.1136/gutjnl-2019-IDDFAbstracts.267

Background Liver biopsy is currently the reference standard for fibrosis staging, but is an invasive procedure with limitations. There are a major unmet need for accurate, readily available noninvasive tests (NITs) to identify patients with advanced fibrosis due to NASH. Our aim is to describe the performance of NITs using the baseline data from the Phase 3 STELLAR studies of the ASK1 inhibitor selonsertib (SEL).

Methods The STELLAR studies (NCT03053050 and NCT03053063) enrolled patients with bridging fibrosis (F3) or compensated cirrhosis (F4) due to NASH (NAFLD Activity Score [NAS] ≥ 3). Baseline liver biopsies were centrally read according to the NASH CRN fibrosis classification and noninvasive markers of fibrosis, including the NAFLD fibrosis score (NFS), Fibrosis-4 (FIB-4) index, Enhanced Liver Fibrosis (ELF) test, and liver stiffness (LS) by transient elastography (TE; FibroScan®) were measured. The performance of these tests to

Abstract IDDF2019-ABS-0133 Table 1 Diagnostic performance of nits to discriminate advanced fibrosis F3-F4

Test	Prevalence of F3-F4	AUROC (95% CI)	Cut-off	Sensitivity	Specificity	PPV	NPV
NFS n=2309	78%	0.75 (0.75, 0.75)	≥ -1.455 ≥ 0.676	90% 39%	37% 89%	83% 93%	52% 30%
FIB-4 n=3125	71%	0.78 (0.78, 0.78)	≥ 1.3 ≥ 2.67	82% 36%	57% 93%	83% 93%	56% 37%
ELF n=3183	71%	0.80 (0.80, 0.80)	≥ 9.8 ≥ 11.3	74% 20%	73% 98%	87% 95%	53% 33%
LS by TE n=1760	84%	0.80 (0.79, 0.8)	≥ 9.9 kPa ≥ 11.4 kPa	83% 75%	61% 71%	92% 93%	41% 36%