Lanifibranor therapy reduces the FAST score

associated with histological 'NASH resolution and improvement of fibrosis' and biomarker response

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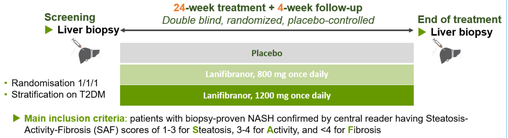
INTRODUCTION & AIM

Lanifibranor, a pan-PPAR agonist, has shown efficacy on the histological endpoint 'NASH resolution and improvement of fibrosis' in the phase 2b NATIVE trial.

We evaluate the effect of lanifibranor on the FibroScan-aspartate aminotransferase (FAST) score, a promising non-invasive test (NIT) for active NASH with significant fibrosis, and its correlation with histological and biomarker response in NATIVE-enrolled patients with F2-F3 fibrosis.

METHOD

Patients with non-cirrhotic NASH and SAF-activity score 3-4 enrolled in NATIVE (n=247) received lanifibranor 800, 1200 mg/d or placebo for 24 weeks.



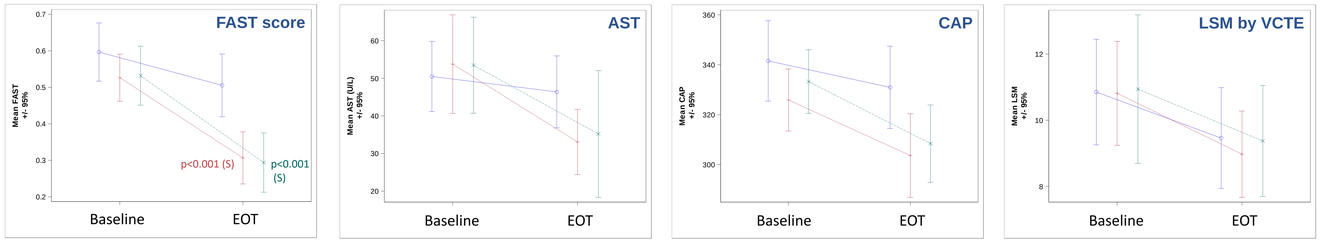
A total of 112 patients had baseline F2-F3 fibrosis and FAST scores available at baseline and end of treatment (EOT).

FAST combines liver stiffness measurement (LSM) by vibration controlled transient elastography (VTCE), controlled attenuation parameter (CAP) and aspartate aminotransferase (AST) levels and provides the probability (between 0 and 1) for active NASH with significant fibrosis (NAS≥4 with at least one in steatosis, lobular inflammation and ballooning and F≥2): ≥0.65: high-risk, 0.35-0.65: intermediate-risk, ≤0.35: low-risk.

FAST scores were compared between lanifibranor and placebo arms using a mixed model adjusted for baseline value; the correlations between changes in FAST scores at EOT and liver histology and biomarkers of metabolism, inflammation and fibrosis were also evaluated.

RESULTS (1/2)

Values over time on F2-F3 patients with available FAST data, over time



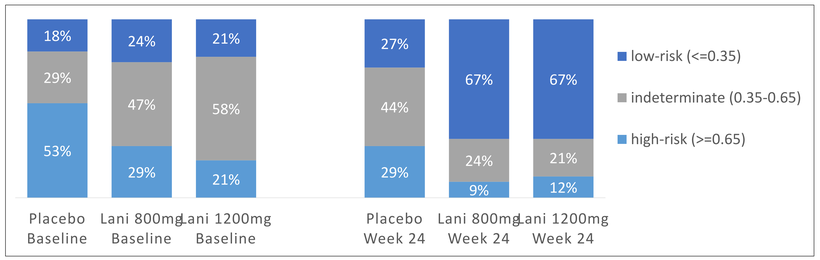
Placebo, Lanifibranor 800mg/d, Lanifibranor 1200mg/d

Pvalues obtained from MMRM adjusted on baseline values, comparing each treatment group to placebo

FAST score was comparable at baseline between treatment groups.

Significant decreases of FAST score were observed at EOT under lanifibranor compared to placebo, mainly driven by the decrease of AST and CAP under lanifibranor compared to placebo.

Probability for active NASH with significant fibrosis, over time

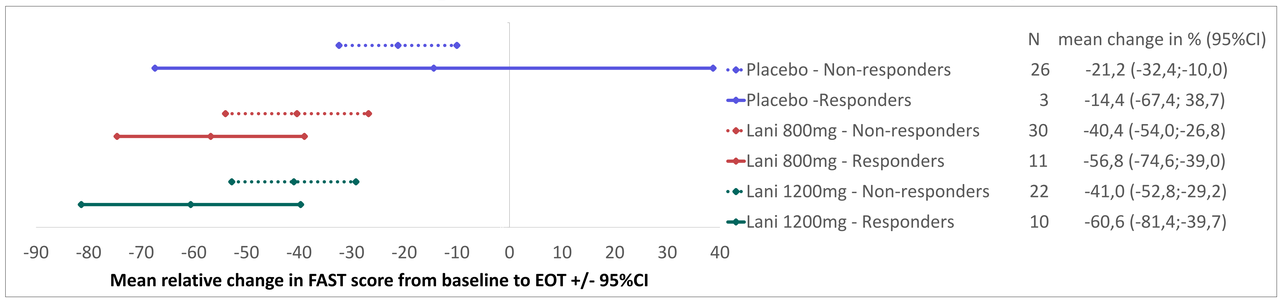


At baseline, similar proportions of patients with low-risk probability were observed in all treatment arms.

At EOT, 67% of patients under lanifibranor were at low-risk versus 27% under placebo.

Lani: Lanifibranor

Correlation between relative change in FAST score and 'NASH resolution and improvement of fibrosis'



Greater reductions in FAST scores were observed among histological responders versus histological non-responders, when considering the histological endpoint 'NASH resolution and improvement of fibrosis'.

RESULTS (2/2)

Correlation between relative changes in FAST score and biomarkers in treated patients

Biomarker	Spearman pvalue
Triglycerides	P<0.001
Apo-C3	P=0.041
Ferritin	P=0.012

Decrease in FAST score correlates with improvement in triglycerides, Apo-C3 and ferritin level.

CONCLUSIONS

Treatment of NASH patients with F2-F3 fibrosis with lanifibranor for 24 weeks leads to a significant reduction of the FAST score compared to placebo and this decrease correlates with improvements in liver histology and biologically relevant biomarker responses. These results not only support the histological efficacy data but also the potential of the FAST score as a NIT to monitor disease progression and response to therapy.

ACKNOWLEDGEMENTS

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