

Cooreman MP<sup>1</sup>, Abdelmalek MF<sup>2</sup>, Baudin M<sup>1</sup>, Huot-Marchand P<sup>1</sup>, Dzen L<sup>1</sup>, Fournier C<sup>3</sup>, Junien JL<sup>1</sup>, Broqua P<sup>1</sup>, Francque S<sup>4</sup>

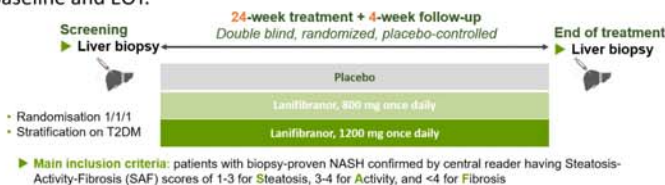
1 INVENTIVA, Daix, France. 2 Division of Gastroenterology and Hepatology, Duke University, Durham, USA. 3 ECHOSENS, Paris, France. 4 Department of Gastroenterology and Hepatology, Antwerp University Hospital, Belgium.

## 1-INTRODUCTION

The pan-PPAR agonist lanifibranor has shown therapeutic efficacy on both NASH resolution and fibrosis improvement in the phase 2b NATIVE study. The primary efficacy endpoint was  $\geq 2$  points decrease of the SAF Activity score, which assesses lobular inflammation and ballooning separately from steatosis. Here we report the efficacy of lanifibranor on steatosis and its correlation with markers of lipid and glucose metabolism.

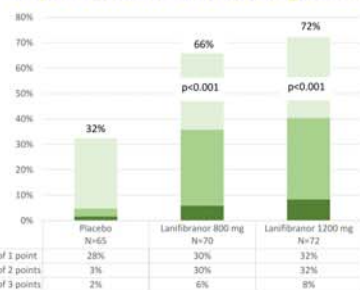
## 2-MATERIAL/METHODS

NATIVE evaluated lanifibranor 800 and 1200 mg/d versus placebo in 247 patients with non-cirrhotic NASH for a treatment duration of 24 weeks. Liver biopsy was obtained at baseline and at the end of treatment (EOT). Histological grading of steatosis was evaluated according to the NASH CRN scoring system. Controlled Attenuation Parameter (CAP) by FibroScan, and serum biomarkers of lipid and glucose metabolism were also performed at baseline and EOT.



## 3-RESULTS

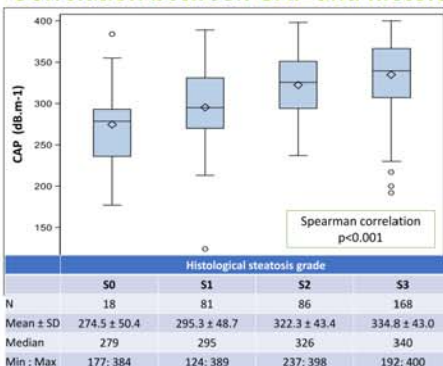
### Improvement of histological steatosis grade



Significant improvements of histological steatosis grade were observed after 24 weeks under lanifibranor compared to placebo, with more than 35% of at least 2 stages improvers in both lanifibranor arm, versus 5% in placebo.

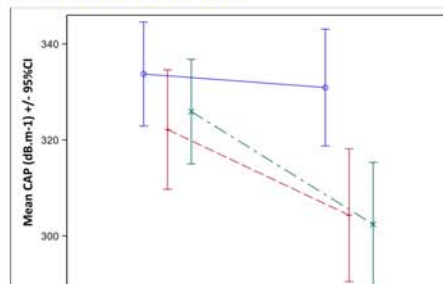
P-values are calculated using a Cochran-Mantel-Haenszel test stratified by diabetic status at baseline.

### Correlation between CAP and histological steatosis grade



Significant relationship between CAP and histological steatosis grade was observed at screening and EOT (Week 24) (pooled data, all treatment confounded).

### Mean CAP over time



	Screening			End of treatment		
	Placebo	Lani 800mg	Lani 1200mg	Placebo	Lani 800mg	Lani 1200mg
N	60	60	54	68	67	64
Mean $\pm$ SD	335 $\pm$ 42	323 $\pm$ 48	326 $\pm$ 39	328 $\pm$ 47	309 $\pm$ 55	304 $\pm$ 50
Median	333	327	326	338	304	300
Min; Max	242; 400	192; 400	241; 400	213; 400	124; 400	177; 400
Pvalue* vs. Placebo	-	0.253 (NS)	0.226 (NS)	-	0.028 (S)	0.005 (S)

### CAP $\leq 302$ dB/m at EOT

	Placebo	Lani 800mg	Lani 1200mg
N screening	53	54	46
CAP $\leq 302^a$ dB/m	14 (26.4%)	16 (29.6%)	15 (32.6%)
Pvalue <sup>b</sup> vs. Placebo	-	0.711 (NS)	0.499 (NS)
N EOT	53	54	46
CAP $\leq 302^a$ dB/m	13 (24.5%)	25 (46.3%)	23 (50.0%)
Pvalue <sup>b</sup> vs. Placebo	-	0.019 (S)	0.009 (S)

Lani=Lanifibranor, <sup>a</sup>youden optimal cutoff of the CAP as a diagnosis marker of Steatosis  $\geq 51$  versus 50. Reference: Accuracy of FibroScan Controlled Attenuation Parameter and Liver Stiffness Measurement in Assessing Steatosis and Fibrosis in Patients With Nonalcoholic Fatty Liver Disease. Gastroenterology. 2019 May;156(6):1717-1730. doi: 10.1053/j.gastro.2019.01.042. Epub 2019 Jan 25. PMID: 30689971, Eddowes P and Ai, <sup>b</sup>Chi<sup>2</sup> test.

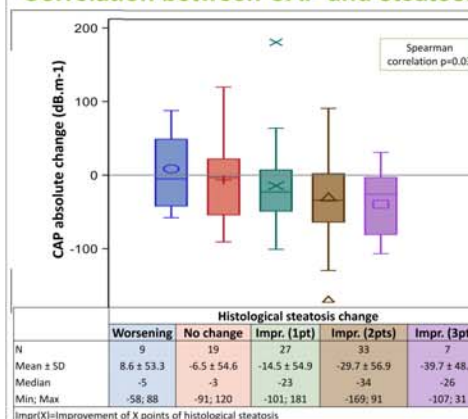
CAP was comparable at baseline between treatment groups.

Significant decreases of CAP were observed at EOT (Week 24) under lanifibranor compared to placebo.

CAP category distribution was comparable at baseline between treatment groups. Significantly higher proportion of patients had CAP<sub>EOT</sub>  $\leq 302$  dB/m in the active groups than in the placebo arm.

### Patients treated with lanifibranor

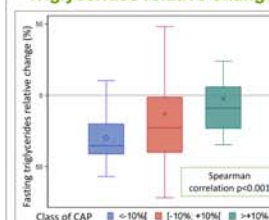
### Correlation between CAP and steatosis grade changes



Significant relationship between change in CAP and change in histological steatosis grade was observed at EOT (Week 24).

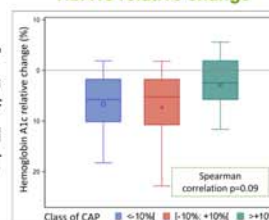
### Correlation between CAP and biomarkers

#### Triglycerides relative change



Decrease in CAP correlates with improvement of triglycerides and HbA1c at EOT (Week 24).

#### HbA1c relative change



## 4-CONCLUSION

Lanifibranor induced a significant reduction in hepatic steatosis, assessed by histology and by CAP, after 24 weeks of treatment. Histological steatosis grading showed a good correlation with CAP by FibroScan in the NATIVE study. Changes in CAP over time also correlated with changes in histological grading of steatosis as well as with improvements of markers of glucose and lipid metabolism.

## Contact information

Michael P COOREMAN  
[Michael.COOREMAN@inventivapharma.com](mailto:Michael.COOREMAN@inventivapharma.com)