

inventiva Lanifibranor-associated adiponectin increase correlates with improvement of histological and serum markers of NASH severity both in terms of activity and fibrosis

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1-INTRODUCTION

Lanifibranor has shown efficacy on liver histology and markers of cardiometabolic health (CMH) in patients with pre-cirrhotic NASH. We previously showed that increases in adiponectin (ADP) with lanifibranor correlated with improvement of CMH markers. We further analysed the correlation between ADP increase and lanifibranor for 1) histological features of NASH severity, and 2) biomarkers of active NASH and fibrosis.

2-MATERIAL/METHODS

The phase 2 NATIVE study evaluated lanifibranor 800 and 1200 mg/d versus placebo in 247 patients for 24 weeks⁽¹⁾.

Paired samples for histological efficacy were available from 211 patients (72 on placebo, 66 and 73 on lanifibranor 800 and 1200 mg). Serum levels of ADP, pro-C3, and MACK-3 score (a score for active and fibrotic NASH calculated from HOMA-IR, aspartate aminotransferase [AST] and cytokeratin 18 [CK-18]) were measured at baseline (BL) and end of treatment (EOT).

BL ADP levels were divided into low, medium and high (<5, 5-10 and >10 ug/mL); ADP increase at EOT was defined as unchanged, moderate and high (<1.5-fold, 1.5-4-fold and >4-fold change). Histological NASH activity grading (steatosis, inflammation, ballooning) and fibrosis staging were per NASH-CRN and SAF scoring. Histological endpoints were NASH resolution and no worsening of fibrosis (E1), improvement of fibrosis and no worsening of NASH (E2), and NASH resolution AND fibrosis improvement (E3).

3-RESULTS

BL ADP levels were low across groups.

Adiponectin (µg/mL) at BL	Placebo	Lanifibranor			
		800 mg	1200 mg	Pooled	lotal
Ν	81	80	83	163	244
Mean (SD)	5.3 ± 4.2	5.0 ± 3.1	5.1 ± 3.2	5.1 ± 3.2	5.1 ± 3.5
Median	4.6	4.2	4.4	4.3	4.5
[Min ; Max]	1.2; 30.8	1.3; 22.3	0.8; 14.7	0.8; 22.3	0.8; 30.8

ADP increase at EOT							
Fold Adiponectin at	Placebo	Lanifibranor					
W24		800 mg	1200 mg	Pooled			
N	72	66	73	139			
Mean (SD)	1.1 ± 0.3	3.8 ± 3.1	4.5 ± 3.5	4.2 ± 3.3			
Median	1.0	2.8	3.5	3.0			
[Min ; Max]	0.1; 2.5	0.8; 18.1	0.7; 17.4	0.7; 18.1			
Unchanged	65 (90%)	9 (14%)	4 (5%)	13 (9%)			
Fold [1.5 - 4]	7 (10%)	38 (58%)	38 (52%)	76 (55%)			
Fold >4	0 (0.0%)	19 (29%)	31 (42%)	50 (36%)			
Nith lanifibranor, ADP increase at EOT correlated with all histological							



References:

[1] S.M. Francque and al. A Randomized, Controlled Trial of the Pan-PPAR Agonist Lanifibranor in NASH. *N Engl J Med.* 2021;385:1547-58.

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ADP increase with lanifibranor in patients with NASH correlated with improvement of histological and serum markers of NASH activity and fibrosis, further supporting that the observed improvements correlate with lanifibranor target engagement. ADP, across the spectrum of NASH, is a biomarker of lanifibranorassociated treatment.

Degree of ADP increase, both absolute and categorical, correlated with