Lanifibranor improves markers of cardiometabolic health in patients with NASH and Type 2 Diabetes, correlated with responses in adiponectin levels

BACKGROUND / OBJECTIVE

Lanifibranor, a pan-PPAR agonist, has shown efficacy on liver histology and metabolic-immune markers of NASH in the phase 2b NATIVE study.\(^1,2\) PPAR signaling is involved in common pathways of NASH and type 2 diabetes (T2D). Adiponectin (ADP) is a pleiotropic adipokine which improves insulin resistance (IR), lipid metabolism, inflammation and fibrosis; low ADP levels are associated with risk for cardiovascular disease and NASH.

RESULTS (1/2)

METHODS AND MATERIAL

NATIVE evaluated lanifibranor 800 and 1200 mg/d versus placebo (PBO) in 247 patients with non-cirrhotic NASH for 24 weeks of treatment. 103 patients had T2D, 144 did not have T2D of whom 47 had prediabetes. In each diabetic subgroup, we evaluated ADP at baseline (BL) and end of treatment (EOT), and correlation between ADP change and prediabetes defined by fasting glucose levels (FGL) versus placebo (PBO) in 247 patients with non-cirrhotic NASH and type 2 diabetes.

In the lanifibranor-treated group, ADP folds increase were similar in the 3 groups, with mean 4.3 folds, versus no increase in the placebo-treated group. Baseline ADP levels were lower in patients with T2D versus patients with prediabetes or normal FGL.

In the pooled lanifibranor arms, increase of ADP folds correlated with improvements in glycemic control, IR, lipid metabolism, and measures of systemic inflammation, consistently in the 3 groups, with higher improvements in patients with T2D and prediabetes compared to the NFGL group.

RESULTS (2/2)

METHODS AND MATERIAL

NATIVE evaluated lanifibranor 800 and 1200 mg/d versus placebo (PBO) in 247 patients with non-cirrhotic NASH for 24 weeks of treatment. 103 patients had T2D, 144 did not have T2D of whom 47 had prediabetes. In each diabetic subgroup, we evaluated ADP at BL and AD and fold at EOT, and correlation between AD change and response of markers.

RESULTS (1/2)

Baseline ADP levels were lower in patients with T2D compared to patients with prediabetes or normal FGL (NFGL).

REFERENCES

S. Francque et 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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DISCUSSION & CONCLUSION

While PPARα and PPARδ agonists have demonstrated pleiotropic effects on HDL cholesterol, apolipoprotein B and CRP, those effects are not associated with an increase in ADP.\(^3\) While other PPARs (through PPARγ) also improve IR and glycemic control, an additional effect on PPARα has a further beneficial impact on these markers, as well as others as shown.

In the patients in this study, baseline ADP levels were low, and treatment with the pan-PPAR agonist lanifibranor significantly improved ADP levels. This increase was correlated with improvement of markers of cardiometabolic health in patients with T2D and prediabetes.

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*3 patients with BL FGL>6.9 mmol/L are not presented here