First clinical evaluation in Chronic Hepatitis B patients of the synthetic Farnesoid X Receptor agonist EYP001


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BACKGROUND

EYP001 is a selective, synthetic FXR agonist being developed for liver diseases, in particular chronic Hepatitis B Virus (HBV) infection

Ex vivo data showed that EYP001 analogue inhibits HBV replication in hepatocytes derived from a mouse model of chronic HBV infection

RESULTS

Safety and tolerability

• EYP001 administration is safe and well tolerated, no serious AEs were observed.
• 45 treatment-emergent AEs (TEAes) occurred, of which 18 were categorized as possibly drug-related. All were of mild intensity except one moderate.
• The most common AEs were gastrointestinal.
• No clinically significant changes in liver enzymes nor lipids occurred.

Pharmacokinetics

• PK parameter: Single oral dose of EYP001 was administered in the morning or in the evening in fasted or fed conditions.
• Food increased T max, but did not change maximum and overall exposure (as expressed by C max and AUC) or elimination (t 1/2).

PD - biomarkers of the FXR-regulated pathway

• Despite rapid elimination kinetics, EYP001 induced prolonged FXR engagement over at least 12 hours under all conditions, as shown by FGF19 increase and C4 decrease.
• FGF19 and C4 PD profiles were similar across fasted and fed conditions. Differences between morning and evening dosing appeared on C4.
• TBA levels were decreased in a fasted state, and rose after a meal, consistent with the bile acid physiology.

PD - HBV vireology

• HBV markers did not change significantly and were not affected by dosing condition.

DISCUSSION AND CONCLUSIONS

In CHB patients EYP001, an oral non-bile salt synthetic FXR agonist.
• was safe and well tolerated and with similar PK profiles for fasted or fed, morning and evening dosing.
• engaged FXR evidenced by FGF19, C4 and TBA changes, with in particular a prolonged C4 decrease with evening dosing.
• No significant effect on HBV markers was detected after single oral EYP001 doses. However an in silico model built in line with recent guidance to FDA [2], showed an inhibitory effect of EYP001 on HBV replication with prolonged treatment (Fig 4).
• A phase Ib study with 4 week EYP001 administration is ongoing.

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REFERENCES


This Clinical Study is registered at ClinicalTrials.gov, Identifier NCT03320616

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