PEVIFOSCORVIR SODIUM DEMONSTRATES PROFOUND ANTIVIRAL ACTIVITY IN UNTREATED HBeAg POSITIVE SUBJECTS, REGARDLESS OF BASELINE ALT LEVEL

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EASL CONGRESS Barcelona Spain 27–30 May 2026

WED-602

INTRODUCTION

Pevifoscorvir sodium (PEVY; ALG-000184) is a prodrug of the capsid assembly modulator (CAM-E) ALG-001075 and has demonstrated potent, pan-genotypic antiviral activity in vitro through a dual mechanism of action: inhibition of HBV pregenomic RNA encapsidation and blockade of cccDNA establishment and replenishment at higher concentrations. [1]

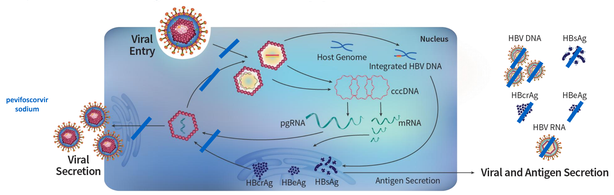

Figure 1: Mechanism of Action of Pevifoscorvir Sodium

In a multipart Phase 1 study (ALG-000184-201), pevifoscorvir sodium 300 mg once daily (QD), with or without entecavir, demonstrated favorable safety and potent antiviral activity in treatment-naïve (TN) or currently-not-treated (CNT) participants with chronic HBV infection.[2,3]

OBJECTIVE

To assess whether baseline ALT level impacts safety or antiviral activity of pevifoscorvir sodium 300 mg QD monotherapy in HBeAg-positive participants.

METHODS

- A total of 10 TN/CNT participants were enrolled and received open-label, oral QD 300 mg PEVY monotherapy for 96 weeks. (Figure 2)

Figure 2: Cohort Design for Oral QD 300 mg PEVY Monotherapy

- Throughout the study, safety assessments (adverse events [AEs], vital signs, electrocardiogram [ECG] and laboratories), PK, and viral biomarkers were collected at regular intervals. The Study Review Committee (SRC) and ALT Flare Committee (AFC) provided oversight of safety by reviewing safety and PK data on a regular basis.
- HBV biomarkers were analyzed at Sonic Laboratory. The Lower Limit of Quantification (LLOQ) and Detection (LOD) of HBV DNA are 10 IU/mL and ≤ 4.92 IU/mL, respectively. LLOQs of HBV RNA, HBsAg, HBeAg and HBcrAg are 10 copies/mL, 0.05 IU/mL, 0.01 PEI U/mL and 3 $\log_{10}$ U/mL, respectively.
- Safety and antiviral activity were compared between low-ALT group (BL ALT < 1.2xULN, n=5) and high-ALT group (BL ALT ≥ 1.2 x ULN, n=5) in a post hoc analysis. (ALT ULN=30 U/L for female and 40 U/L for male)

CONTACT INFORMATION

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BASELINE CHARACTERISTICS

- The baseline demographic and disease characteristics are comparable between 2 groups.

TABLE 1: Baseline Characteristics

TN/CNT HBeAg+ Participants receiving 300 mg PEVY monotherapy	Low-ALT group n=5	High-ALT group n=5
Age, years, mean (SEM)	33.8 (4.7)	35.8 (3.8)
Female, N(%)	2 (40)	1 (20)
Asian, N(%)	5(100)	4 (80)
BMI, kg/m^2, mean (SEM)	22.2(1.0)	22.5 (1.3)
HBV Genotype, N(%)	B:4(80), C:1(20)	B:1(20), C:3(60), D:1(20)
HBV DNA, $\log_{10}$ IU/mL, mean (SEM)	7.8(0.4)	8.2 (0.3)
HBV RNA, $\log_{10}$ copies/mL, mean (SEM)	5.2(0.5)	5.4 (0.8)
HBsAg, $\log_{10}$ IU/mL, mean (SEM)	4.4(0.2)	4.2(0.2)
HBeAg, $\log_{10}$ PEI U/mL, mean (SEM)	2.7(0.4)	2.6(0.4)
HBcrAg, $\log_{10}$ U/mL, mean (SEM)	8.2(0.3)	8.4(0.2)
ALT, U/L, mean (SEM)	35.0 (2.6)	86.4 (16.6)

SAFETY

TABLE 2: Safety Summary

TN/CNT HBeAg+ Participants receiving 300 mg PEVY monotherapy	Low-ALT group n=5	High-ALT group n=5
Numbers of subjects with		
at least one TEAE, n (%)	4(80)	5(100)
SAE	0	0
TEAE leading to study drug discontinuation	0	0
TEAE Grade ≥ 3*, n(%)	2(40)	1(20)

*All Grade ≥3 TEAEs were ALT/AST elevation with preserved synthetic and excretory liver functions. All events resolved in the setting of continued pevifoscorvir sodium dosing and were not considered clinically concerning by the ALT Flare Committee.

ANTIVIRAL ACTIVITY

TABLE 3: Mean (SEM) Changes From Baseline in HBV Markers at Week 48 and 96 During 300 mg PEVY Monotherapy

TN/CNT HBeAg+ Participants receiving 300 mg PEVY monotherapy	Low-ALT group n=5	High-ALT group n=5
HBV DNA $\log_{10}$ IU/mL (SEM)		
Week 48	-6.6(0.4)	-7.2(0.2)
Week 96	-6.8(0.4)	-7.2(0.3)
HBV RNA $\log_{10}$ copies/mL (SEM)		
Week 48	-4.2(0.5)	-4.4(0.8)
Week 96	-4.2(0.5)	-4.4(0.8)
HBsAg $\log_{10}$ IU/mL (SEM)		
Week 48	-0.8(0.2)	-0.6(0.3)
Week 96	-1.0(0.3)	-0.7(0.3)
HBeAg $\log_{10}$ PEI U/mL (SEM)		
Week 48	-1.2(0.2)	-2.0(0.2)
Week 96	-1.7(0.2)	-2.4(0.2)
HBcrAg $\log_{10}$ U/mL (SEM)		
Week 48	-1.2(0.2)	-1.9(0.3)
Week 96	-1.8(0.2)	-2.5(0.3)

TN-treatment naïve; CNT-currently not treated; ULN-upper limit of normal; BMI-body mass index

Figure 3: Mean HBV Antigen Changes (SEM) from Baseline in TN/CNT HBeAg+ Participants receiving 300 mg PEVY Monotherapy

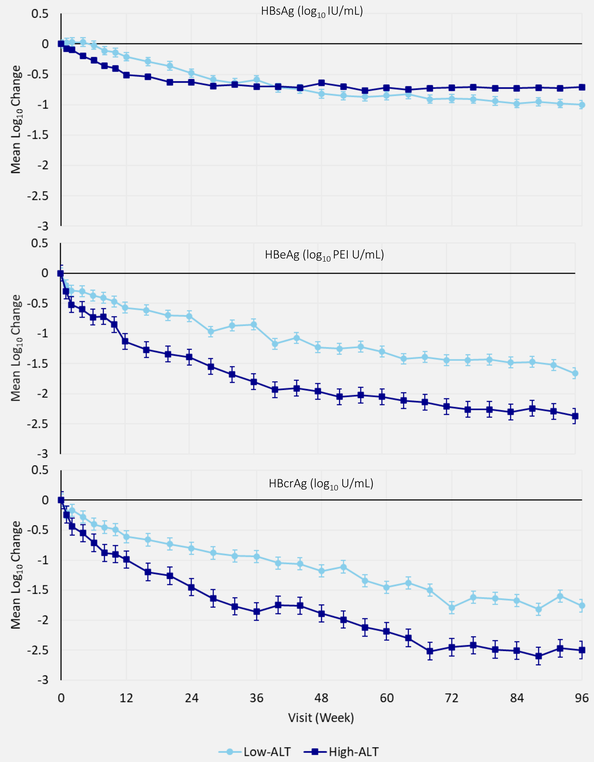


TABLE 4: Proportion of TN/CNT HBeAg+ Participants Achieving HBsAg Level < 3000 IU/mL at Week 48, Stratified by Baseline HBsAg Level

Baseline HBsAg Level#	ALT Groups	N	Participants with HBsAg < 3000 IU/mL at Week 48 n (%)
3000-10000 IU/mL	Low-ALT	1	0
	High-ALT	2	0
> 10000 IU/mL	Low-ALT	4	2(50)
	High-ALT	3	2(66.7)
All	Low-ALT	5	2(40)
	High-ALT	5	2(40)

N: total participant number in each ALT group; n: participant number with HBsAg < 3000 IU/mL at Week 48 in each ALT group

All 10 TN/CNT HBeAg+ participants with baseline HBsAg level > 3000 IU/mL

Figure 4. Individual HBV DNA Level Over Time in TN/CNT HBeAg+ Participants receiving 300 mg PEVY Monotherapy

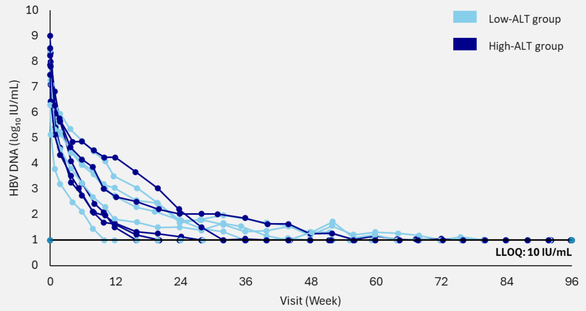
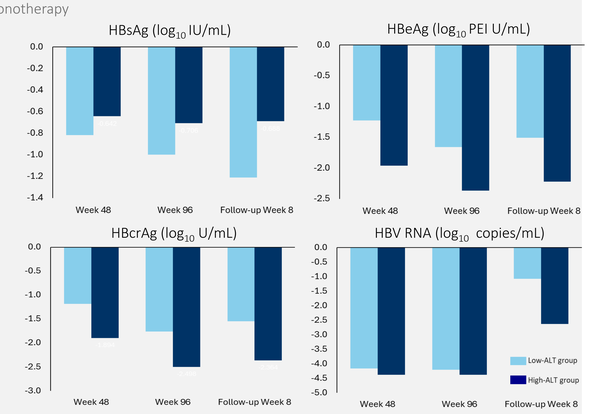


Figure 5. Mean HBV RNA and HBV Antigen Changes from Baseline Including NA Only 8-Week Follow-up between Low- and High- ALT TN/CNT HBeAg+ Participants with 300 mg PEVY Monotherapy



Low-ALT group, n=	5	5	3^
High-ALT group, n=	5	5	5

^ Exclude 2 participants who did not initiate NA treatment at the end of PEVY monotherapy.

- **300 mg PEVY monotherapy for 96 weeks demonstrated in TN/CNT HBeAg+ participants with low and high ALT at baseline demonstrated:**
  - **Favorable safety profile**
  - **Similar rapid, profound, and durable reduction in HBV DNA and HBV RNA in both groups, without viral breakthrough (Table 3, Figure 4)**
  - **HBV DNA LLOQ < 10 IU/mL (TD or TND) and HBV RNA LLOQ < 10 copies/mL were achieved by Week 96 in all participants**
  - **Multiple log reduction in HBV antigens were observed in both groups (Table 3, Figure 3). The reductions in HBeAg and HBcrAg were greater in the High-ALT group than that in the Low-ALT group**
  - **Notably, among all participants with baseline HBsAg ≥ 3000 IU/mL, 40% (4/10) achieved HBsAg < 3000 IU/mL at Week 48 (Table 4), suggesting eligibility for a functional cure combination regimen, which may include an antisense oligonucleotide (ASO) agent.**
- **After 96-week PEVY monotherapy, during 8-week NA only follow-up period (Figure 5):**
  - **HBV antigen reductions were sustained in both groups**
  - **HBV RNA moderately increased, with increases in the high ALT group less than in the Low-ALT group**
- **Further evaluation is ongoing in the Phase 2, B-SUPREME study (NCT06963710)**

REFERENCES 1. Ling EASL 2020; 2. JL Hou APASL 2025; 3. MF Yuen AASLD 2025;