Sustained Reduction of HBV Antigen Levels During the 8-Week Follow-up Period in Treatment-Naïve (TN) or Currently-Not-Treated (CNT) HBeAg-Positive Subjects with Chronic Hepatitis B Virus Infection After 96-Week 300 mg ALG-000184, With or Without Entecavir (ETV) Sustained Reduction of HBV Antigen Levels During the 8-Week Follow-up Period in Treatment Naïve (TN) or Currently-Not-Treated (CNT) HBeAg-Positive Subjects with Chronic Hepatitis B Virus Infection After 96-Week 300 mg ALG-000184, With or Without Entecavir (ETV)

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ALIGOS THERAPEUTICS

INTRODUCTION

- Pevifoscorvir sodium (ALG-000184) is a prodrug of the Capsid Assembly Modulator (CAM) E, ALG-001075, which has demonstrated potent, pan-genotypic antiviral activity in vitro through the dual mechanism of action (MOA) [1]:
  - inhibition of pgRNA encapsidation (1st MOA)
  - blocking cccDNA establishment/replenishment at higher concentrations (2nd MOA)
- ALG-000184-201 (NCT04536337) is a multipart Phase 1 study of pevifoscorvir sodium. Preliminary data demonstrated a favorable safety profile and potent antiviral effect, with significant suppression of HBV DNA, HBV RNA, and decline in HBV antigens in treatment-naïve/currently-not-treated (TN/CNT) subjects with chronic Hepatitis B virus (HBV) infection who received ≤ 300 mg pevifoscorvir sodium oral once daily (QD) ± Entecavir (ETV) for ≤ 96 weeks [2,3].

AIM

To evaluate the safety, pharmacokinetics (PK), and antiviral activity following once daily dosing of pevifoscorvir sodium in subjects with chronic HBV infection.

METHOD

- A total of 36 TN/CNT HBeAg+ (HBeAg-positive) subjects were enrolled and randomly received once daily oral doses of 100 mg pevifoscorvir sodium or 300 mg pevifoscorvir sodium or placebo + ETV for 12 weeks, followed by 100 mg pevifoscorvir sodium + ETV or 300 mg pevifoscorvir sodium + ETV for additional 12 or 96 weeks, or received open label 300 mg pevifoscorvir sodium monotherapy for 96 weeks (Figure 1).

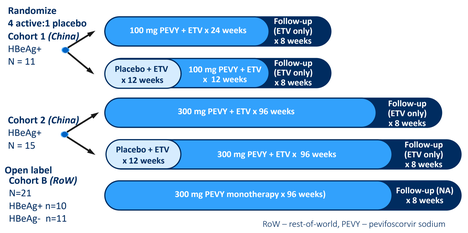

Figure 1: Cohort Design for Long-Term Pevifoscorvir Sodium Treatment

- Here, we present HBV biomarker data in the subjects who completed 24 weeks of 100 mg pevifoscorvir sodium + ETV or 96 weeks of 300 mg pevifoscorvir sodium ± ETV, followed by 8 weeks of NA only
- Virology assays were performed in Sonic Laboratories (Rest-of-World, ROW) and KingMED (China). Lower Limit of Quantitation (LLOQ) of HBV DNA, HBV RNA, HBsAg, HBeAg and HBcrAg assays are 10 IU/mL, 10 or 200 copies/mL, 0.05 IU/mL, 0.01 PEI U/mL or 1 COI and 3 log U/mL, respectively

RESULTS

Part 4 HBeAg+ Subjects	Cohort 1		Cohort 2		Cohort B
pevifoscorvir sodium (PEVY) dose and regimen	100 mg PEVY +ETV	ETV ×12 Weeks followed by 100 mg PEVY+ ETV	300 mg PEVY +ETV	ETV ×12 Weeks followed by 300 mg PEVY+ETV	300 mg PEVY Monotherapy
N	8	3	3	12	10
Age, years, mean (SD)	38 (4.2)	27 (5.0)	28 (4.6)	32.3 (10.2)	34.8 (9.1)
Male, n(%)	3 (37.5)	1 (33.3)	2 (66.7)	6 (50)	7 (70.0)
Asian, n(%)	8 (100)	3 (100)	3 (100)	12 (100)	9 (90.0)
BMI, kg/m², mean (SD)	22.3 (2.9)	21.5 (2.7)	22.3 (2.8)	22.2 (3.1)	22.4 (2.4)
HBV Genotype, n(%)	B: 2 (25) C:6 (75)	C: 3 (100)	B: 1 (33) C: 2 (67)	B: 4 (33) C: 8 (67)	B: 5 (50), C: 4(40), D: 1 (10)
HBV DNA, log_{10} IU/mL, mean (SD)	8.6 (0.3)	8.4 (0.2)	7.8 (1.1)	8.1 (0.8)	8.0 (0.8)
HBV RNA, log_{10} copies/mL, mean (SD)	7.1 (0.5)	7.2 (0.4)	6.5 (0.9)	6.7 (1.1)	5.3 (1.3)
HBsAg, log_{10} IU/mL, mean (SD)	4.7 (0.4)	4.6 (0.2)	4.1 (0.4)	4.5 (0.7)	4.3 (0.5)
HBeAg, log_{10} PEI U/mL, mean (SD)	2.6 (0.03)	2.6 (0.01)	2.0 (0.3)	2.5 (0.3)	2.6 (0.8)
HBcrAg, log_{10} U/mL, mean (SD)	8.5 (0.2)	8.3 (0.06)	8.0 (1.2)	8.3 (0.5)	8.3 (0.6)
ALT, U/L, mean (SD)	18 (5.2)	21.7 (16.7)	38.7 (9.1)	41.5 (22.7)	60.7 (36.9)

SD: standard deviation

Table 2: Baseline Characteristics

HBV biomarker changes during follow-up were analyzed in subjects initially received pevifoscorvir sodium ± ETV and completed 24- or 96-week study treatment, followed by NA only treatment for 8 weeks.

- In Part 4 Cohort 1, 4 of 8 HBeAg+ subjects, who were initially assigned to 100 mg pevifoscorvir sodium+ ETV completed 24 weeks of treatment and 8 weeks of ETV only follow-up.
- In Part 4 Cohort 2: 7 of 12 HBeAg+ subjects, who were initially assigned to 300 mg pevifoscorvir sodium + ETV, completed 96 weeks of treatment and 8 weeks of ETV only follow-up.
- In Part 4 Cohort B: 8 of 10 HBeAg+ subjects completed 96 weeks of 300 mg pevifoscorvir sodium monotherapy and 8 weeks of NA only follow-up.

ANTIVIRAL ACTIVITY – HBV DNA and HBV RNA

- Potent antiviral effect in HBV DNA reduction has been demonstrated in TN/CNT subjects with chronic HBV infection who received up to 300 mg pevifoscorvir sodium ± ETV for 96 weeks. [3,4]
- In subjects who completed treatment (100- mg or 300 mg pevifoscorvir sodium + ETV) and NA only follow-up, a mean HBV RNA reduction of 3.9 log_{10} copies/mL from baseline at Week 24 was observed in both dose regimens.
- Importantly, HBV RNA level was maintained at Week 8 of NA only follow-up in subjects who received 96 weeks of 300 mg pevifoscorvir sodium + ETV, compared with those who received 24 weeks of 100 mg pevifoscorvir sodium + ETV (mean reductions from baseline: 3.2 versus 0.5 log_{10} copies/mL (Figure 2).

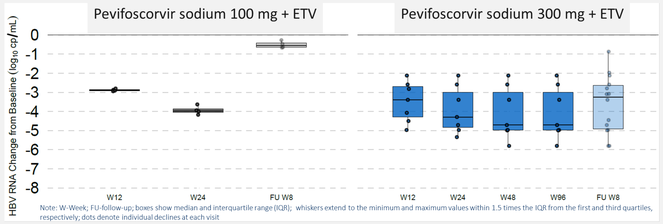

Figure 2: HBV RNA Change from Baseline Over Time During Treatment of 100 mg Pevifoscorvir Sodium + ETV x 24 Weeks (N=4) and 300 mg Pevifoscorvir Sodium + ETV x 96 Weeks (N=7), Followed by NA Only 8 Week Follow-up

ANTIVIRAL ACTIVITY – HBV ANTIGENS

- HBV antigen reduction during pevifoscorvir sodium ± ETV dosing was dose- and duration-dependent (Figures 3, 4)
  - At Week 24, mean HBV antigen reduction in 100 mg and 300 mg pevifoscorvir sodium + ETV were 0.5 and 0.6 log_{10} IU/mL for HBsAg, 0.5 and 0.8 log_{10} PEI U/mL for HBeAg, and 0.6 and 1.2 log_{10} U/mL for HBcrAg, respectively (Figure 3)
  - Decline in HBV antigens continued with 300 mg pevifoscorvir sodium ± ETV dosing. At Week 48 and 96, mean reductions were 0.8 and 0.8 log_{10} IU/mL in HBsAg, 1.6 and 2.0 log_{10} PEI U/mL in HBeAg, and 1.7 and 2.3 log_{10} U/mL in HBcrAg, respectively (Figure 4)
- During the NA only 8-week follow-up period, no apparent HBV antigen increase was observed in subjects who completed 96 weeks of 300 mg pevifoscorvir sodium ± ETV: mean decline at follow up Week 8 was 0.7 log_{10} IU/mL for HBsAg, 1.8 log_{10} PEI U/mL for HBeAg, and 2.0 log_{10} U/mL for HBcrAg (Fig. 5)

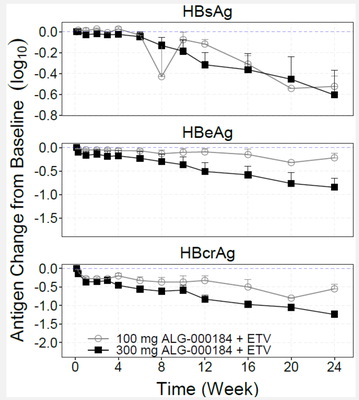

Figure 3: Mean (SEM) HBV Antigen Change from Baseline During 24 Weeks of 100 mg Pevifoscorvir Sodium + ETV (N=4) versus 300 mg Pevifoscorvir Sodium + ETV (N=7)

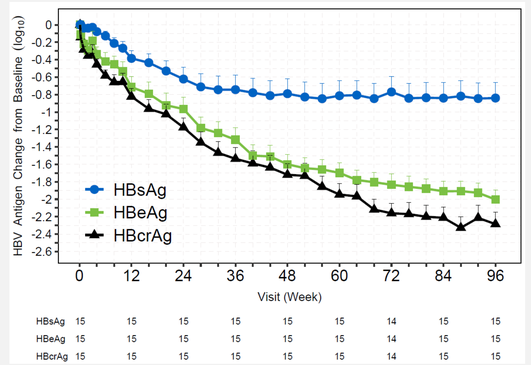

Figure 4: Mean (SEM) HBV Antigen Reduction from Baseline During 96-Week Treatment of 300 mg Pevifoscorvir Sodium ± ETV

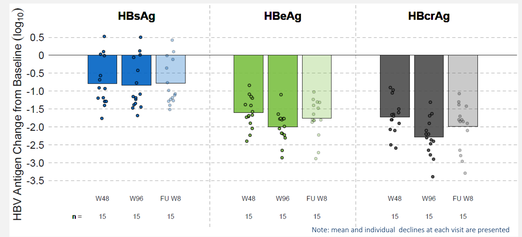

Figure 5: Mean HBV Antigen Changes from Baseline at Week 48, 96 of 300 mg Pevifoscorvir Sodium ± ETV Treatment and Week 8 of NA Only Follow-up

CONCLUSIONS

- **Treatment with 100 mg pevifoscorvir sodium or 300 mg pevifoscorvir sodium with or without ETV in HBeAg+ subjects with chronic HBV infection for 24 or 96 weeks resulted in:**
- **During treatment period**
  - **Pevifoscorvir sodium produced rapid, profound and durable reductions in HBV DNA and HBV RNA with both the 100 and 300 mg dosing regimens**
  - **A dose-related decline in HBV antigens were observed**
  - **Multiple-log reduction in HBsAg, HBeAg, and HBcrAg were noted following 96 weeks of 300 mg pevifoscorvir sodium ± ETV**
- **During NA only 8-week follow-up period**
  - **HBV antigen and HBV RNA reduction was maintained during NA only 8 Week follow up that suggests pevifoscorvir sodium potentially reduces cccDNA pool due to engagement of the CAM-E secondary MOA**

REFERENCES 1. Ling EASL 2020; 2. JL Hou APASL 2025; 3. MF Yuen Oral #0198 AASLD 2025;

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