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PEVIFOSCORVIR SODIUM REDUCES HBSAG LEVELS TO < 3000 IU/ML IN HBEAG POSITIVE PARTICIPANTS WITH CHRONIC HBV INFECTION FOLLOWING LONG TERM TREATMENT

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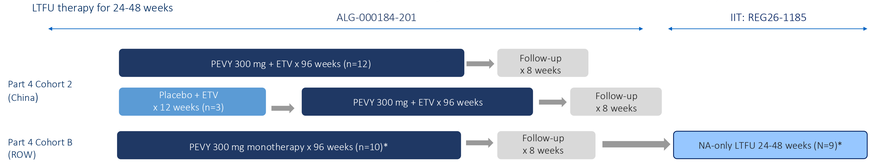
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ALIGOS THERAPEUTICS

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INTRODUCTION

- Pevifoscorvir Sodium (PEVY or ALG-000184) is the prodrug of a potent class E capsid assembly modulator (CAM-E) ALG-001075. PEVY is currently being studied for the treatment of chronic HBV infection.
- ALG-000184-201 (NCT04536337) is a multipart Phase 1 trial, assessing the safety, pharmacokinetics, and antiviral activity of oral pevifoscorvir sodium (PEVY or ALG-000184) 300 mg once daily for up to 96 weeks in participants with chronic HBV infection.
- Here, we report HBsAg reductions in HBeAg+ participants stratified by baseline HBsAg levels after finite treatment with PEVY 300 mg ± entecavir (ETV).
  - We have previously shown that HBeAg+ participants with HBsAg levels of ≥ 10,000 IU/mL have a higher likelihood of strong HBsAg reductions after PEVY 300 mg ± ETV therapy. [1]
  - In the Phase 3 B-well 1 and 2 studies, functional cure was achieved in 19% of noncirrhotic patients with chronic HBV infection with baseline HBsAg levels of 100-3000 IU/mL after 24 weeks with antisense oligonucleotide (ASO) bepirovirsen in combination with stable nucleos/tide (NA) therapy, followed by an additional 24 weeks of NA monotherapy.[2]
- The ad hoc analysis includes participants from ALG-000184-201 (Figure 1):
  - Part 4 Cohort 2 (P4C2): 12 HBeAg+ participants who received PEVY 300 mg + ETV for up to 96 weeks, followed by 8 weeks of NA therapy
  - Part 4 Cohort 2 (P4C2): 3 HBeAg+ participants who after a 12-week lead-in with ETV received PEVY 300 mg + ETV for up to 96 weeks, followed by 8 weeks of NA therapy
  - Part 4 Cohort B (P4CB): 10 HBeAg+ participants who received PEVY 300 mg monotherapy for 96 weeks, followed by 8 weeks of NA therapy
  - The Investigator-Initiated Trial (IIT) REG26-1185 which prospectively followed 9 HBeAg+ participants who, after completion of PEVY monotherapy for 96 weeks in P4CB, were on NA LTFU therapy for 24-48 weeks



n = number of HBeAg-positive participants enrolled in each arm. IIT: investigator-initiated trial. ROW: rest of world. PEVY = pevifoscorvir sodium (ALG-000184).
*LTFU: long-term follow-up; Samples collected during the 96-week PEVY phase, the 8-week FU phase and the LTFU phase of participants enrolled in the LTFU study REG26-1185 were retested for HBV DNA, RNA and antigens at The University of Hong Kong School of Medicine. One participant completed 24 weeks, 7 completed 36 weeks, and 1 completed 48 weeks of NA LTFU

Figure 1. Design of Phase 1 Clinical Trial ALG-000184-201 Part 4 Cohort 2 and B Design and IIT REG26-1185 Long-Term Follow-Up Study

BASELINE DEMOGRAPHICS

Characteristic	ALG-000184-201 Part 4 Cohort 2 and B HBeAg+			REG26-1185 HBeAg+
	Total (N=19)[1]	Low HBsAg (n=5)[2]	High HBsAg (n=14)[3]	LTFU subgroup (n=9)[4]
Age, years	33.1 (2.3)	40.0 (5.2)	30.6 (2.2)	35.7 (3.1)
Weight, kg	62.3 (2.8)	68.1 (5.5)	60.2 (3.3)	67.5 (3.1)
BMI, kg/m2	22.1 (0.6)	23.3 (1.1)	21.7 (0.7)	22.8 (0.7)
Sex, Male, n (%)	11 (58%)	4 (80%)	7 (50%)	7 (78%)
Sex, Female, n (%)	8 (42%)	1 (20%)	7 (50%)	2 (22%)
Race, Asian, n (%)	18 (95%)	5 (100%)	13 (93%)	9 (100%)
Race, White, n (%)	1 (5%)	0 (0%)	1 (7%)	0 (0%)
Baseline HBsAg, $\log_{10}$ IU/mL	4.3 (0.1)	3.5 (0.2)	4.6 (0.1)	4.2 (0.1)
Baseline HBeAg, $\log_{10}$ PEIU/mL	2.5 (0.1)	2.1 (0.3)	2.7 (0.1)	2.6 (0.3)
Baseline HBV DNA, $\log_{10}$ IU/mL	8.0 (0.2)	7.0 (0.3)	8.4 (0.1)	8.0 (0.3)
Baseline HBV RNA, $\log_{10}$ copies/mL	5.9 (0.3)	4.8 (0.6)	6.3 (0.4)	5.2 (0.5)
Baseline HBcrAg, $\log_{10}$ U/mL	8.3 (0.1)	7.8 (0.4)	8.5 (0.1)	8.3 (0.2)
Baseline ALT, U/L	53.6 (7.3)	62.2 (17.2)	50.5 (8.0)	61.9 (13.0)

Table 1: Baseline demographics of HBeAg+ participants in Part 4 Cohorts 2 and B and in the IIT REG26-1185
[1]Excludes 3 participants initially assigned to Placebo + ETV and 3 participants initially assigned to 300 mg PEVY + ETV (dosing duration <12 weeks, n=2; PK-confirmed non-compliance with PEVY dosing, n=1), resulting in HBeAg+ Cohort 2 (300 mg PEVY + ETV, n=9) and HBeAg+ Cohort B (300 mg PEVY monotherapy, n=10). [2]Low HBsAg: participants with baseline HBsAg <4 $\log_{10}$ IU/mL. [3]High HBsAg: participants with baseline HBsAg ≥ 4 $\log_{10}$ IU/mL. [4]LTFU subgroup: 9 Cohort B monotherapy participants with long-term follow-up for 24–48 weeks post-PEVY treatment.

METHODS

HBV marker assays — ALG-000184-201

- Central laboratories: Sonic (rest of the world [ROW] sites) and KingMed (China sites).
- HBV DNA: LLOQ 10 IU/mL; LLOD ≤ 4.92 IU/mL.
- HBV RNA: LLOQ 10 (ROW) or 200 (China) copies/mL.
- HBsAg: LLOQ 0.05 IU/mL. HBeAg: LLOQ 0.01 (ROW) or 0.22 (China) PEI U/mL. HBcrAg: LLOQ 3 $\log_{10}$ U/mL.
- P4C2 and P4CB virology summaries include only participants initially assigned to PEVY 300 mg ± ETV who received > 12 weeks of treatment and were confirmed compliant based on pharmacokinetic analysis.

HBV marker assays — REG26-1185 LTFU cohort

- Assay performed and/ or obtained at the University of Hong Kong School of Medicine
- qHBsAg: Elecsys HBsAg II (Roche Diagnostics); LLOD 0.05 IU/mL.
- qHBeAg: Elecsys HBeAg quant (Roche Diagnostics); LLOD 0.10 IU/mL.
- HBV RNA: RealTime HBV RNA v2.0, RUO (Abbott Diagnostics); LLOQ 0.49 $\log_{10}$ U/mL.
- HBV DNA: Cobas Taqman (Roche Diagnostics); LLOQ 20 IU/mL, LLOD 10 IU/mL.
- HBcrAg: iTACT-HBcrAg Lumipulse immunoassay (Fujirebio); LLOD 2.1 $\log_{10}$ U/mL.

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RESULTS: ALG-000184-201 PART 4 COHORT 2 AND B

Pooled analysis of 19 HBeAg positive participants from ALG-000184-201 Part 4 Cohorts 2 (PEVY ± ETV) and B (PEVY monotherapy) demonstrates that only in participants with a high baseline HBsAg level of ≥ 10,000 IU/mL a clinically meaningful reduction in HBsAg can be achieved after treatment with PEVY 300 mg (**Figure 2**). In contrast, HBsAg concentrations stay largely stable in participants with a baseline HBsAg level of < 10,000 IU/mL. In high baseline HBsAg participants, HBsAg might be transcribed predominately from cccDNA. In vitro, potent CAM-E such as PEVY can reduce the cccDNA pool through the second mechanism of action. [3] In participants with a low HbsAg baseline, HBsAg might be predominately transcribed from integrated DNA, which is not directly affected by PEVY. The effect of PEVY on cccDNA is further supported by significant reductions of HBeAg and HBcrAg, which are only transcribed from cccDNA (**Figure 3**).

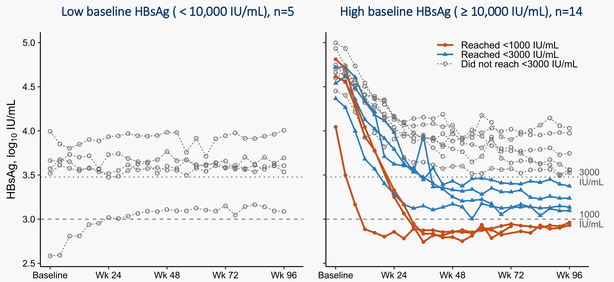


Figure 2. Significant reduction in HBsAg concentrations in HBeAg+ participants in P4C2 (PEVY ± ETV) and P4CB (PEVY monotherapy) with a baseline HbsAg level of < 10,000 IU/mL (left) versus a baseline HBsAg level of ≥ 10,000 IU/mL (right). Participants reaching HBsAg concentrations < 1000 IU/mL (orange), < 3000 IU/mL (blue) after treatment with PEVY 300 mg ± ETV vs participants not reaching HBsAg concentrations of < 3000 IU/mL (grey).

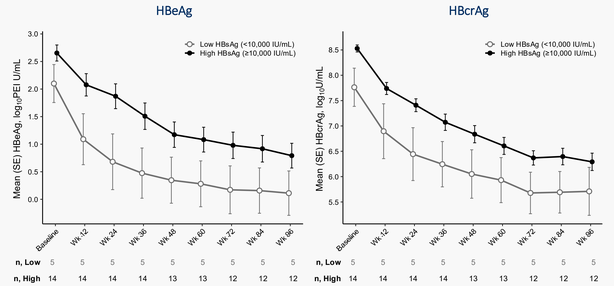


Figure 3. PEVY potently reduces HBeAg and HBcrAg in HBeAg+ participants from P4C2 (PEVY ± ETV) and P4CB (PEVY monotherapy) independently of their baseline HbsAg levels.

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RESULTS: IIT REG26-1185

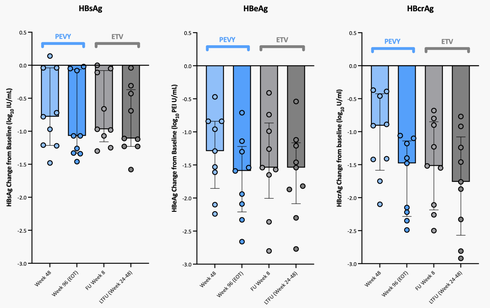


Figure 4. Reductions in HBsAg, HBeAg and HBcrAg observed in 9 HBeAg+ participants during the 96-week treatment with PEVY 300 mg were maintained the NA-only LTFU period.

In 9 HBeAg+ participants of P4CB, which were later enrolled in the IIT REG26-1185, significant reductions in HBsAg, HBeAg and HBcrAg were observed during the treatment with PEVY 300 mg for 96 weeks (**Figure 4, blue bars**). These reductions were maintained during the 8-week NA only FU and LTFU lasting 24-48 weeks (**Figure 4, grey bars**). HBeAg and HBcrAg are exclusively transcribed from cccDNA; in HBeAg+ participants, HBsAg originates predominately from cccDNA. The reductions in these antigens during PEVY treatment are likely caused by a reduction in the cccDNA, as has been shown in vitro.[3] ETV during the FU and LTFU periods is thought to sufficiently suppress viral replication, thereby preventing de novo infection of hepatocytes and limiting the cccDNA pool size.

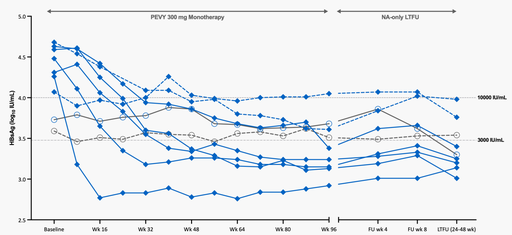


Figure 5. HBsAg reductions of 9 HBeAg+ participants in the LTFU cohort with a baseline HBsAg ≥ 10,000 IU/mL (blue lines) or < 10,000 IU/mL (grey)

6 of 7 HBeAg+ participants in the LTFU cohort with a baseline HBsAg > 10,000 IU/mL (Figure 5, blue lines) achieved a > 1 $\log_{10}$ reduction in HBsAg after 96-week of PEVY 300 mg treatment, while the HBsAg concentrations of 2 participants (**Figure 5, grey lines**) with low baseline HBsAg levels remained unchanged. 6 of 9 participants had HBsAg levels < 3000 IU/mL after the LTFU (**Figure 5, solid lines**), theoretically achieving entry eligibility criteria for a functional cure regimen containing an ASO such as bepirovirsen. Of these 6 participants, 5 had baseline HBsAg levels of > 10,000 IU/mL.

Baseline HBsAg Level	N	Number of Participants with HBsAg < 3000 IU/mL (%)		
		At 48 weeks of PEVY ± ETV	At 96 weeks of PEVY ± ETV	At 24-48 weeks of ETV LTFU after 96 weeks of PEVY
3000-10,000 IU/mL	5	0/5 (0%)	0/5 (0%)	1/3 (33%)
> 10,000 IU/mL	15	9/15 (60%)	6/12 (50%)	5/6 (83%)
All	20	9/20 (45%)	6/17 (35%)	6/9 (67%)

Table 2. Participants with a high baseline HBsAg concentration have a higher likelihood to achieve HBsAg of < 3000 IU/mL after treatment with PEVY 300 mg; Weeks are counted from the first PEVY dose; the 3 participants in the 12-week placebo + ETV lead-in started PEVY at study Week 12. One of these participants completed treatment after 36 weeks of PEVY; their last on-treatment value (Week 36) was carried forward to Week 48.

Finite treatment with PEVY 300 mg ± ETV results in substantial reductions of HBsAg, especially in participants with baseline HbsAg levels of > 10,000 IU/mL. After 48 weeks of PEVY 300 mg ± ETV, 60% of participants with a high HBsAg baseline but none with a low HBsAg baseline reduced HBsAg levels to < 3000 IU/mL (Table 2).

CONCLUSION

- **The extent in HBsAg reduction during PEVY monotherapy and combination therapy with ETV was dependent on baseline HBsAg levels with substantially higher reductions of HBsAg in participants with baseline HBsAg levels > 10,000 IU/mL.**
- **Of these participants, 9/15 (60 %) achieved HBsAg < 3000 IU/mL at Week 48, suggesting potential eligibility for a functional cure combination regimen, that might include an antisense oligonucleotide agent such as bepirovirsen.**
- **Reductions in HBsAg observed during PEVY monotherapy were maintained during LTFU with ETV for 24-48 weeks**

REFERENCES 1. Kha L et al., EASL 2024 (Poster Wed-378), 2. Hou J et al., N Engl J Med 2026; 394: 2395-406, 3. Debing Y et al., International HBV Meeting 2025