

ALG-000184 (100 mg) + ETV Leads to Stronger Antiviral Effects Compared to ETV Alone in HBeAg-Positive CHB

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Disclosure



- Member of Scientific Advisory Board for GlaxoSmithKline, Gilead Science, Aligos
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Background



- Capsid assembly modulators which produce empty viral particles (CAM-E) have 2 antiviral mechanisms of action:
 - Inhibition of capsid assembly, leading to reductions in HBV DNA and RNA levels
 - Prevention of cccDNA establishment/replenishment, leading to reductions in antigens (e.g., HBsAg)
- ALG-000184 (oral prodrug of CAM-E, ALG-001075) is currently being evaluated in a multipart, randomized, double-blind Phase 1 study (ALG-000184-201*), including in untreated CHB subjects
- Part 4 is evaluating 100-300 mg ALG-000184 with or without ETV in HBeAg+ and HBeAg- CHB subjects
 - The safety and pharmacodynamics of treatment with 100 mg ALG-000184 + ETV x ≤24 weeks (Part 4 Cohort 1) have not previously been reported and are being presented here

ALG-000184-201 Part 4 Study Design









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ALG-000184-201 Part 4 Cohort 1 Key Study Entry Criteria



Adult subjects with chronic HBV infection

- Treatment naïve
- HBeAg positive
- ALT and AST \leq 1.2 × ULN
- HBV DNA $>10^{7}$ IU/mL
- HBsAg ≥ 100 IU/mL
- Metavir scrore < F3 or liver stiffness measurment < 8.5 kPa

ALG-000184-201 Part 4 Cohort 1 Baseline Characteristics



	100mg ALG-000184 + ETV	ETV
	N=8	N=3
Age, years, mean (SEM)	38 (1.5)	27 (2.9)
Male, N (%)	3 (37.5)	1 (33.3)
Asian, N (%)	8 (100)	3 (100)
BMI, kg/m², mean (SEM)	22.3 (1.0)	21.5 (1.6)
HBeAg positive, N (%)	8 (100)	3 (100)
HBV Genotype B/C, N (%)	B: 2 (25); C: 6 (75)	C: 3 (100)
HBV DNA, log ₁₀ IU/mL, mean (SEM)	8.6 (0.1)	8.4 (0.1)
HBV RNA, log ₁₀ copies/mL, mean (SEM)	7.1 (0.2)	7.2 (0.2)
HBsAg, log ₁₀ IU/mL, mean (SEM)	4.7 (0.1)	4.6 (0.1)
HBeAg, log ₁₀ PEI U/mL, mean (SEM)	2.6 (0.0)	2.6 (0.0)
HBcrAg, log ₁₀ U/mL, mean (SEM)	8.5 (0.1)	8.3 (0.0)
ALT<1.2 x ULN, N (%)	8 (100)	3 (100)

Typical profile for HBeAg+ subjects with chronic HBV infection

ALG-000184-201 Part 4 Cohort 1 Mean HBV DNA Change Over Time





At Week 12, an additional 1.3 log₁₀ HBV DNA decline was observed with ALG-000184 + ETV vs. ETV alone After Week 12, there is a rapid decline after adding on ALG-000184 to ETV monotherapy At Week 24, both arms achieved similar nadir levels (reductions of -6.4 vs. -6.8 log₁₀ IU/mL) After stopping ALG-000184, but continuing ETV, DNA rose by 1.2-1.6 log₁₀ IU/mL, but remained suppressed

ALG-000184-201 Part 4 Cohort 1 Mean HBV RNA Change Over Time





At Week 12, there was a 2.8 log₁₀ HBV RNA decline with ALG-000184 + ETV vs. no change with ETV After Week 12, a steep HBV RNA decline occurs after adding on ALG-000184 to ETV At Week 24, both arms achieved similar RNA levels After stopping ALG-000184 dosing, but continuing ETV, HBV RNA returned to near baseline levels

ALG-000184-201 Part 4 Cohort 1 HBV Antigens Change Over Time





Through Week 12, mean antigen levels declined in ALG-00184 + ETV arm vs. no change with ETV alone Antigen levels only declined in setting of dosing with ALG-000184 After stopping ALG-000184, but continuing ETV, mean antigen levels rebounded

ALG-000184-201 Part 4 Cohort 1 Safety



Ν	100mg ALG-000184/PBO + ETV	
	N=11	
Serious Adverse Event (SAE)	0	
Treatment Emergent Adverse Event (TEAE) leading to study drug discontinuation	0	
Grade ≥3 TEAE	0	
Concerning laboratory, electrocardiogram, vital sign, or physical examination findings	None	

100 mg ALG-000184 <u>+</u> ETV x ≤24 weeks was well tolerated

Conclusion



100 mg ALG-000184 + ETV x \leq 24 weeks in untreated HBeAg+ subjects with chronic HBV infection:

- Demonstrated a favorable safety profile
- Resulted in superior antiviral activity (HBV DNA & RNA) compared to ETV alone
- Lowered HBV antigens vs. no effect on antigens with ETV alone
- After stopping ALG-000184 dosing (but continuing ETV), all viral markers (HBV DNA, HBV RNA and HBV antigens) rebounded

Additional data in this study are presented in:

- Oral 101807: 300mg ALG-000184 ± ETV x ≤68 weeks in HBeAg-positive CHB subjects
- Oral 101816: Ethnic effects on safety & PD among HBeAg-negative CHB subjects dosed with 10-50mg ALG-000184 alone for 28 days