
# ALG-000184 Has Favorable Antiviral Effect & Safety in Untreated Asian/Non-Asian HBeAg-Negative CHB Subjects

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# Disclosure

- Member of Scientific Advisory Board for AbbVie, Abbott Diagnotics, Aligos Therapeutics, AiCuris, Antios Therapeutics, Arbutus Biopharma, Arrowhead Pharmaceuticals, Assembly Biosciences, Clear B Therapeutics, Dicerna Pharmaceuticals, Finch Therapeutics, Fujirebio Incorporation, GlaxoSmithKline, Gilead Sciences, Immunocore, Janssen, Precision BioSciences, Roche, Sysmex Corporation, Tune Therapeutics, Vir Biotechnology and Visirna Therapeutics.

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# Background

- ALG-000184 is a capsid assembly modulator-empty (CAM-E), which inhibits HBV via
  - Primary mechanism: promotes premature assembly of core protein, resulting in empty capsids and reductions of HBV DNA/RNA
  - Secondary mechanism: prevents the establishment/replenishment of cccDNA, resulting in reductions of HBcrAg, HBeAg, and HBsAg

- Study ALG-000184-201 (NCT04536337) is an ongoing multi-part Phase 1 study evaluating oral dosing with ≤300 mg ALG-000184 in healthy volunteers and CHB subjects
  - Single/multiple ALG-000184 doses in healthy volunteers (Parts 1 & 2) were well tolerated with a favorable PK profile
    - › No ethnic differences in PK or safety between Asian and non-Asian healthy volunteers were observed[1]
  - Dosing with ≤300 mg ALG-000184 x 28 days in HBeAg+ and HBeAg- CHB subjects was well tolerated, with favorable PK, and potent antiviral activity demonstrated[2]
    - › Effect of ethnicity on ALG-000184 PK, safety, and antiviral activity in CHB subjects has not been previously evaluated

1. Ed Gane HBV-TAG 2021; 2. Gane et al., APASL 2023

# ALG-000184 Part 3 Study Design


- Randomized, double blind, placebo controlled
- Each cohort (N=10/cohort) was randomly assigned (4 active: 1 placebo) to dose x 28 days
- Population: untreated HBeAg+ and HBeAg- CHB subjects
- Dose levels evaluated by population

| ALG-000184 Dose Level (mg) | HBeAg Status |
|---|---|
| 10 | HBeAg- |
| 50 | |
| 100 | |
| 10 | HBeAg+ |
| 100 | |
| 300 | |

# ALG-000184 Part 3
# Key Study Entry Criteria


## Adult subjects with CHB or chronic HBV infection

- Treatment naïve or currently not treated
- HBeAg positive or negative
- ALT and AST ≤5 × ULN
- HBV DNA >2000 IU/mL
- Metavir scrore < F3 or liver stiffness measurment < 8.5 kPa

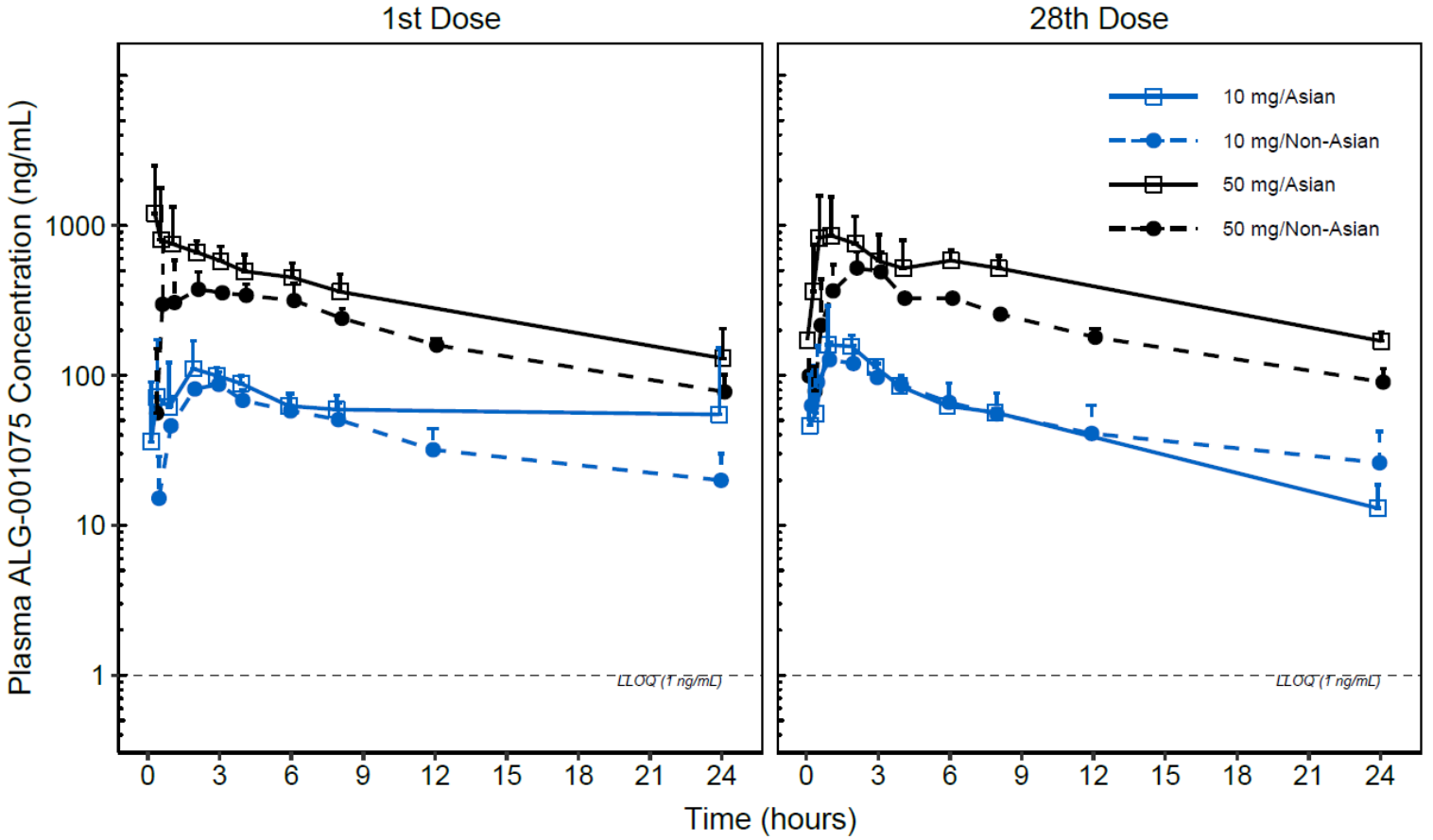
# Baseline Characteristics of ALG-000184 Treated Subjects


| Dose level | HBeAg Negative | | | | | | HBeAg Positive |
|---|---|---|---|---|---|---|---|
| | ALG-000184 Dose | | | | | | ALG-000184 Dose 10-300mg N=25 |
| | 10mg N=7 | | 50mg N=8 | | 100mg N=8 | | |
| | Asian | non-Asian | Asian | non-Asian | Asian | Non-Asian | Asian |
| n | n=3 | n=4 | n=5 | n=3 | n=1 | n=7 | n=25 |
| Age, years, mean (SEM) | 46.3 (1.3) | 42.2(3.0) | 48(3.3) | 34(3.1) | 56 | 42.4(3.1) | 32.8(1.2) |
| Male, N(%) | 1(33) | 1 (25) | 3(60) | 1(33) | 0 | 3(43) | 14/25(56) |
| BMI, kg/M2, mean (SEM) | 24.5(6.7) | 27.0 (0.3) | 23.3 (2.1) | 27.9(7.5) | 23.3 | 27.7(2.2) | 22.1(0.6) |
| HBV genotype: A/B/C/D/E (%) | A:1(33) B: 2(67) | D: 4(100) | B: 4(80) C:1(20) | A:1(33) D:2(67) | B:1(100) | A:1(14) D:6(86) | B:13(52) C:12(48) |
| HBV DNA, $log_{10}$ IU/mL mean (SEM) | 4.0(0.2) | 4.2(0.2) | 4.8(0.6) | 4.7(0.5) | 4.1 | 4.2(0.5) | 8.4(0.1) |
| HBV RNA, $log_{10}$ copies/mL mean (SEM) | 1.3(0.8) | 1.2(0.4) | 2.1(0.6) | 2.1(0.5) | 1.8 | 1.6(0.5) | 7.8(0.2) |

Sufficient Asian/non-Asian data available for analysis only in HBeAg- subjects dosed with 10, 50 mg ALG-000184

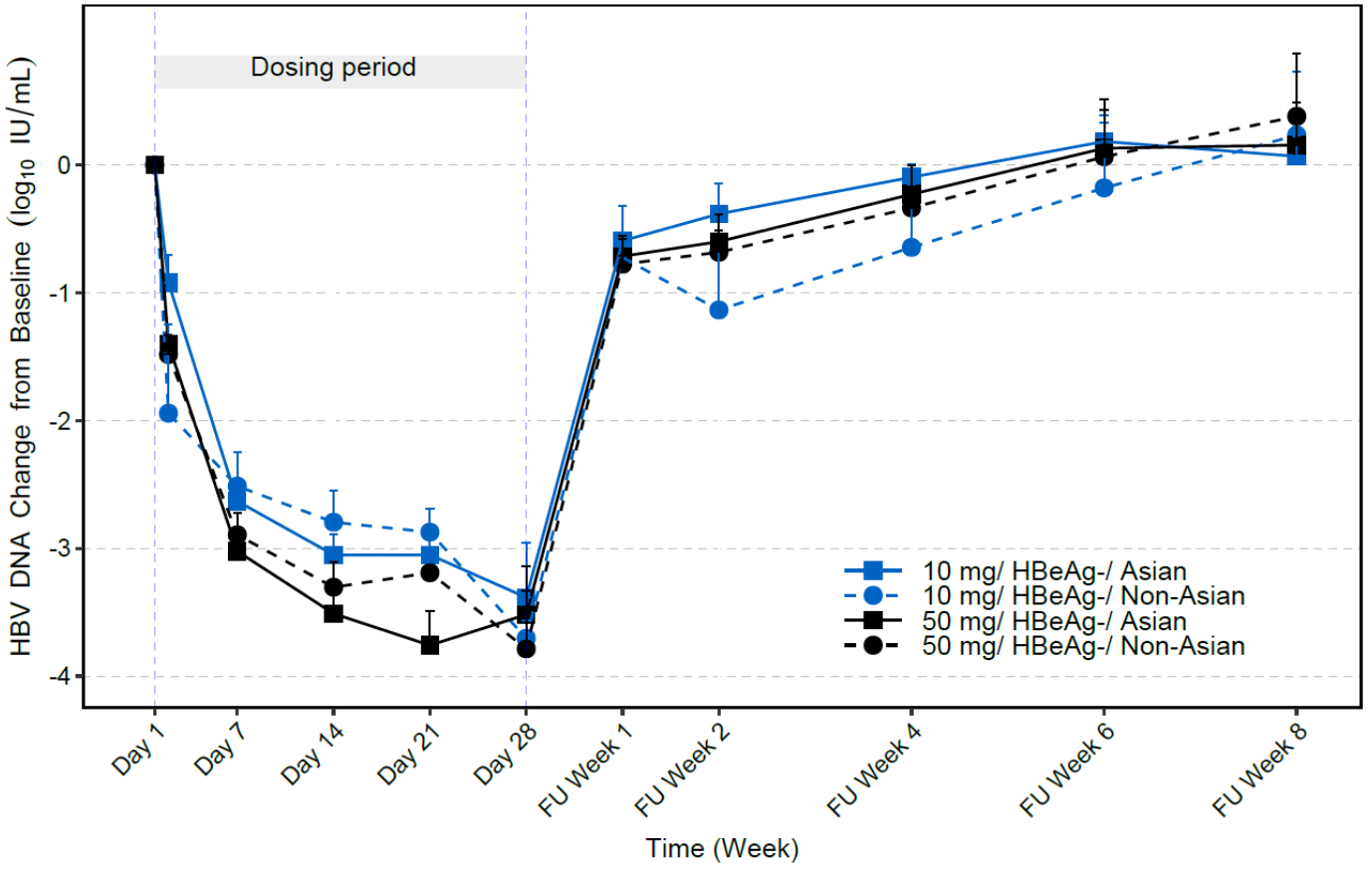
# ALG-001075 Plasma Pharmacokinetics Asian vs Non-Asian in HBeAg (-)





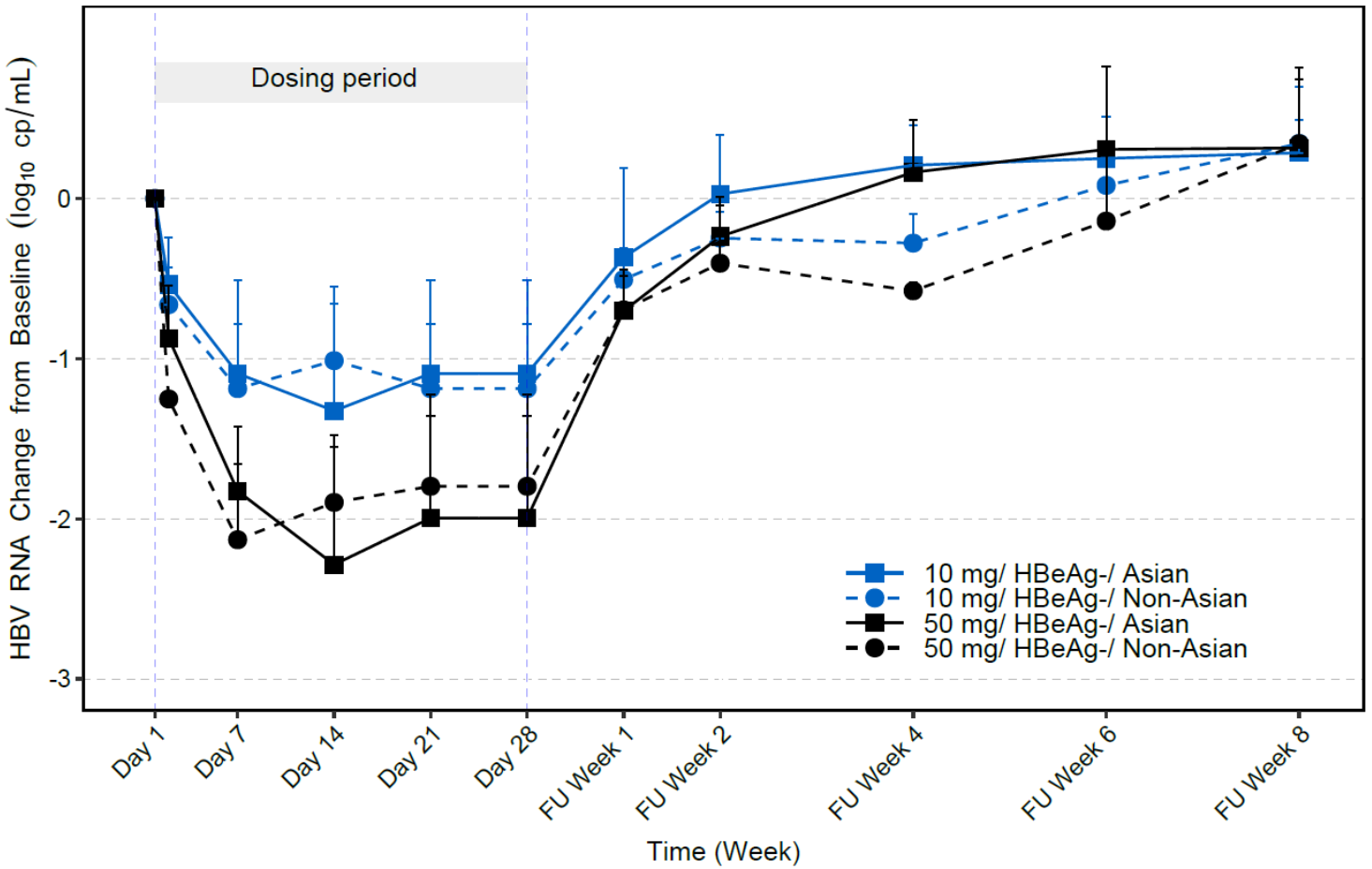

After adjusting for dose and bodyweight, there was a ~2-fold increase in $C_{max}$ and AUC observed for Asian vs. non-Asian subjects on Days 1 and 28

# HBV DNA Changes Over Time Asian vs Non-Asian in HBeAg(-)




Similar HBV DNA reductions seen in 50 mg vs. 10 mg cohorts
No meaningful DNA differences seen in either cohort between Asian and non-Asian subjects
Similar number of Asians (5/8) and non-Asians (3/7) had HBV DNA < LLOQ (10 IU/mL) at Day 28

# HBV RNA Changes Over Time Asian vs Non-Asian in HBeAg(-)


Greater HBV RNA reductions seen in 50 mg due to high baseline level
No RNA differences seen in either cohort between Asian and non-Asians subjects
All Asians (7/7) and non-Asians (5/5) with available data at Day 28 had HBV RNA < LLOQ (10 IU/mL)

# Safety
# Asian vs non-Asian in HBeAg(-)


| Dose | 10 mg | | 50 mg | |
|---|---|---|---|---|
| N | 7 | | 8 | |
| Subject, N(%) | Asian n=3 | Non-Asian n=4 | Asian n=5 | Non-Asian n=3 |
| Any TEAE | 1 | 0 | 3 (60) | 3 (100) |
| SAE | 0 | 0 | 0 | 0 |
| TEAE leading to study drug discontinuation | 0 | 0 | 0 | 0 |
| Grading | | | | |
| TEAE Grade 1 | 1(33) | 0 | 3 (60) | 2 (67) |
| TEAE Grade 2 | 0 | 0 | 0 | 3 (100) |
| TEAE Grade ≥3 | 0 | 0 | 0 | 0 |

ALG-000184 was well tolerated in HBeAg-negative subjects dosed daily with 10-50 mg ALG-000184 x 28 days
Similar safety profile between Asian and non-Asian subjects

# Conclusion


- Dosing with 10 or 50 mg ALG-000184 x 28 days was associated with small ~2x fold differences in drug concentrations between Asian and non-Asian HBeAg- subjects
- Asian and non-Asian HBeAg- CHB subjects dosed with 10 and 50 mg ALG-000184 had a similar safety profile and had similar reductions in HBV DNA and RNA
- Long term dosing (≤96 weeks) of HBeAg- and HBeAg+ CHB subjects with ≤300 mg ALG-000184 is ongoing

Additional data in this study ALG-000184-201 are presented in:

- Oral 101807 for Part 4 Cohort 2 and B: 300mg ALG-000184 ± ETV in HBeAg-positive CHB subjects for up to 72 weeks
- Oral 101816 for Part 4 Cohort 1: 100mg ALG-000184 + ETV in HBeAg-positive CHB subjects for up to 24 weeks