Safety, Pharmacokinetics (PK), and Antiviral Activity of the Capsid Assembly Modulator (CAM) ALG-000184 in Asian and non-Asian Subjects with Chronic Hepatitis B (CHB)

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INTRODUCTION

Worldwide, more than 260 million people are affected by Chronic Hepatitis B (CHB) and approximately 820,000 people per year die from cirrhosis and hepatocellular carcinoma (HCC) due to CHB. Long-term treatment with current standard of care for CHB, nucleus (cidofovir) suppresses HBV replication and reduces liver injury in most patients, but rarely results in functional cure, the goal of CHB treatment. Therefore, there is a significant medical need for novel approaches to enhance functional cure rates. ALG-000184 is a produg of ALG-000135, a novel, pan-genotypic CAM that reduces viral capsid assembly and preserves efficacy.

AIM

To evaluate the safety, PK, and antiviral activity of multiple doses of ALG-000184 in Asian and non-Asian CHB subjects.

MATERIALS AND METHODS

ALG-000184-201 is a three-part, multicenter, double-blind, randomized, placebo-controlled Phase 1 study conducted in China, Hong Kong, New Zealand, Moldova, and United Kingdom (NCT04536337).

• Parts 1 and 2: all subjects have completed dosing and follow up
• Single oral doses up to 500 mg and multiple oral doses (7 days) up to 250 mg were evaluated in healthy volunteers (N=48) and were found to be well tolerated with dose dependent linear PK in both Asian and non-Asian subjects.
• Part 3 is ongoing and evaluating multiple cohorts (N=10/cohort; 8 active: 2 placebo) of currently not treated/nucleoside/nucleotide/nucleoside or positive CHB subjects, who receive daily (QD) oral doses of ALG-00184 for 28 days, after which they are followed up for 8 weeks
• Key Inclusion Criteria: ALT and AST ≤ 5 x ULN; HBV DNA > 2000 IU/mL
• Key Exclusion Criteria: Liver fibrosis classified as Metavir A/B/C/D/unknown, (%)

BASELINE CHARACTERISTICS

Across the cohorts, Asian CHB subjects had a lower BMI, a higher prevalence of HBeAg positivity, a different predominant HBV genotype, and a higher mean HBV HBV DNA and HBV RNA compared to non-Asian subjects.

RESULTS

Similar rapid and substantial declines in HBV DNA and HBV RNA were observed at the 100 mg and 50 mg dose levels, regardless of HBeAg status (Fig. 1). The Asian vs. non-Asian analysis was feasible for Cohort 2 only, as in Cohort 1 only one subject was Asian and all subjects in Cohort 4 were Asian.

ANTIVIRAL ACTIVITY

● No significant difference in exposures by body weight adjusted doses was observed between Asian and non-Asian subjects

CONCLUSIONS

● Oral dosing for 28 days with 100 mg and 50 mg of ALG-00184/placebo was generally well tolerated among both Asian and non-Asian subjects.

● Similar rapid declines in HBV DNA and HBV RNA were observed at both 50 mg and 100 mg dose levels, regardless of HBeAg status. No significant difference in antiviral activity were noted between Asian and non-Asian subjects receiving 50 mg ALG-00184 and 100% of subjects had HBV RNA < LLOQ.

● No significant difference in exposures by body weight adjusted doses was observed between Asian and non-Asian subjects

Dosing in additional cohorts is ongoing. A Phase 2 study to evaluate combinations of ALG-00184 with other novel therapeutics is planned.

ACKNOWLEDGMENTS

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