The safety and efficacy of hepalatide（L47）treatment combined with pegylated interferon-alpha 2a in patients with chronic hepatitis B: the preliminary data from a double-blind, RCT phase II trial

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Introduction

Hepalatide（L47）, a 47aa synthetic peptide derived from Hepatitis B virus (HBV) Pre-S1, can blocks HBV entry into hepatocytes by competitively binding to HBV entry receptor sodium taurocholate co-transporting polypeptide (NTCP) on the surface of hepatocytes.

Aim

The aims of this study were to explore the safety and efficacy of hepalatide in the treatment-naïve patients with chronic hepatitis B (CHB).

Method

This randomized, placebo-controlled, double-blind phase 2 clinical trial (NCT 04426968) was planned to enroll 96 treatment-naïve CHB patients with HBV DNA ≥ 20000 IU/mL(HBeAg(+)) or HBV DNA ≥ 2000 IU/mL(HBeAg(-)), 2×ULN≤ALT≤10×ULN from 12 hospitals in China. The CHB patients were randomly assigned to three groups with different open-label L47 doses (group A 2.10mg, group B 4.20mg, and group C 6.30 mg). In each group, patients were double-blindly randomized to receive L47 or placebo treatment in a 3:1 ratio. All patients received subcutaneous injections of L47 or placebo once-daily, combined with subcutaneous injections of pegylated interferon-alpha 2a (PegIFN) (180μg/Week) for 24 weeks, then followed up for 24 weeks with PegIFN treatment alone(Fig 1). The primary endpoint is HBV DNA loss (cut-off value 20 IU/mL at the end of 24 weeks).

Conclusions

Though the study is not complete, the preliminary data show a good safety and well tolerance of L47 treatment in combination with Peg-IFN. Importantly, the HBV DNA levels were declined rapidly in a L47 dose-dependent manner, highlighting its therapeutic potential in anti-HBV treatment.

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Results

Safety

As of December 26, 2022, 22 enrolled patients (including 19 patients with HBeAg positive and 3 patients with HBeAg negative) have completed 24-week combination treatment (group A, n=7; group B n=8; group C, n=7). The uncovered preliminary data showed that, in all groups, the adverse events (AEs) were generally grade 1 or 2, and most were identified to be related to PegIFN, such as fever, headache, fatigue, leukocytosis, neutropenia. No treatment-related serious AEs were reported.

Mean levels of HBV DNA, HBsAg and ALT decreased significantly from baseline in all three groups(Fig2).

The baseline HBV DNA levels in the three groups were 8.29±0.61 log IU/mL, 7.34±1.42 log IU/mL and 7.69±0.58 log IU/mL, respectively. At 12 weeks of treatment, the HBV DNA levels were declined by 2.39±1.28 log IU/mL in group A, 2.21±1.53 log IU/mL in group B and 4.23±1.8 log IU/mL in group C, respectively. At the end of 24-week treatment, the HBV DNA levels were further declined by 3.70±2.02 log IU/mL, 2.82±1.71 log IU/mL, 4.54±1.62 log IU/mL in the three groups, respectively.

The levels of quantitative hepatitis B surface antigen (qHBsAg) were declined from baseline by 1.36±0.99 log IU/mL, 0.89±0.79 log IU/mL, 0.70±0.76 log IU/mL IU/mL in the three groups at the end of 24-week treatment, respectively.

The ALT normalization rate was 28.6%, 37.5% and 57.1% in the three groups at the end of 24-week treatment, respectively.

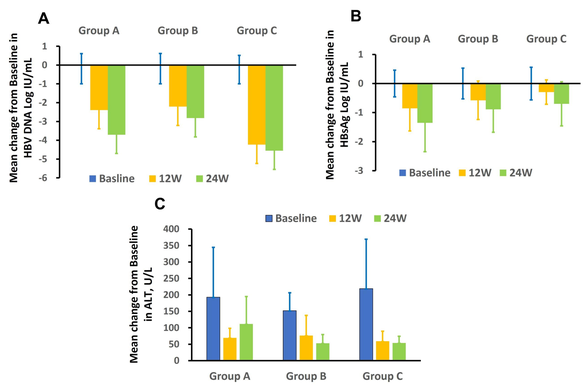

Fig 2. Mean Change from Baseline in HBV DNA, HBsAg and ALT

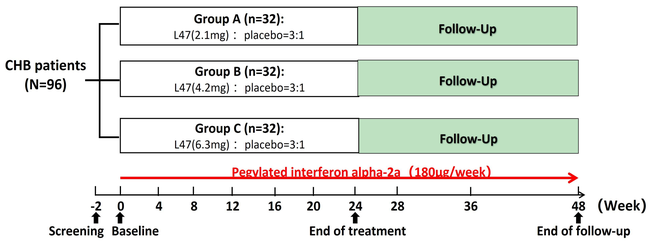

Fig 1. Study Designs

Individual Changes of HBV DNA, HBsAg and ALT in all three groups(Fig3).

One patient in group A and one patient in group B reached primary endpoint. one patient achieved HBsAg loss (below 0.05 IU/mL) with presence of hepatitis B surface antibody, one patient achieved HBeAg seroconversion.

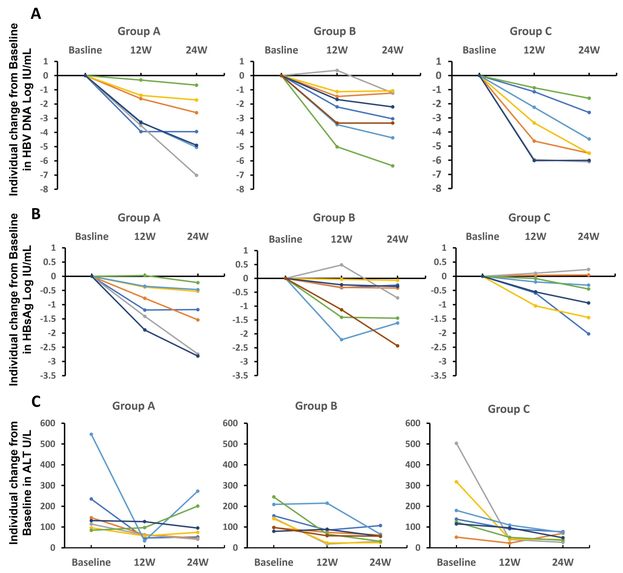

Fig 3. Individual Change from Baseline in HBV DNA, HBsAg and ALT