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Efficacy and Safety of PD-L1 Antibody ASC22 (Envafolimab) in Patients with Low Baseline HBsAg Levels: a randomized Phase IIb Expansion Cohort

Guiqiang Wang[1], Guoxin Hu[2], Lei Fu[3], Jiajie Lu[4], Yongping Chen[5], Qing Xie[6], Yao Xie[7], Guizhou Zou[8], Xiaolin Guo[9], Jinlin Hou[10], Yongfeng Yang[11], Qianguo Mao[12], Yuemei Yan[13], Jinzi J. Wu[13]

1. Peking University First Hospital; 2. Peking university Shenzhen hospital; 3. Xiangya Hospital of Central South University; 4. West China Hospital of Sichuan University; 5. The First Affiliated Hospital of Wenzhou Medical University; 6. Ruijin Hospital of Medical College of Shanghai Jiaotong University; 7. Beijing Ditan Hospital Capital Medical University; 8. The Second Affiliated Hospital of Anhui Medical University; 9. The first hospital of Jilin University; 10. Nanfang Hospital of Southern Medical University; 11. Nanjing Second Hospital; 12. Xiamen Hospital of Traditional Chinese Medicine; 13. Ascletis BioScience Co., Ltd.

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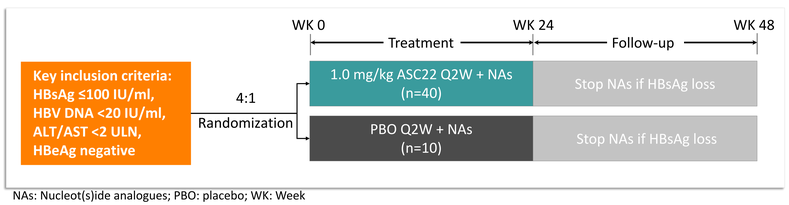
Background

A Phase 2b study demonstrated the potential of the subcutaneously injected PD-L1 antibody ASC22 to reduce HBsAg levels in patients with chronic hepatitis B (CHB). This effect was particularly notable in patients with low baseline (BL) HBsAg (≤100 IU/mL), where 43% (3/7, per-protocol set) achieved a functional cure. An expansion cohort has been planned to further validate the efficacy and safety profile of ASC22 in this specific subpopulation.

Methods

The design of this randomized, single-blind, multi-center, Phase IIb extension cohort study is shown in Figure 1.

Figure 1: Study design



NAs: Nucleot(s)ide analogues; PBO: placebo; WK: Week

Results

The patient population was predominantly male (79.6%), with a median age of 46 years. The mean ALT level was 22.7 U/L, and the mean HBsAg level was 27.8 IU/mL, as shown in Table 1.

Table 1. Baseline characteristics and demographics

Characteristics	1.0mg/kg ASC22 + NAs (N=40)	PBO + NAs (N=9)	Total (N=49)
Male, n(%)	33(82.5%)	6(66.7%)	39(79.6%)
Age, Median(range)	46.0(36.8,52.0)	47.0(38.0,53.0)	46.0(37.0,52.0)
BMI (kg/m^2), Mean(SD)	23.6(2.6)	24.5(1.9)	23.8(2.5)
ALT (U/L), Mean(SD)	22.6(10.6)	22.9(14.5)	22.7(11.3)
AST (U/L), Mean(SD)	23.7(7.2)	22.1(3.2)	23.4(6.7)
HBsAg(IU/mL), Mean(SD)	28.9(28.3)	22.9(26.0)	27.8(27.7)
pgRNA(copies/mL), Mean(SD)	555.0(2168.5)	198.3(227.7)	489.5(1961.8)
HBcrAg(log$_{10}$ U/mL), Mean(SD)	3.2(0.4)	3.5(0.8)	3.3(0.5)
Duration of NAs treatment (years), Median(range)	5.6(3.1,18.0)	9.0(4.8,12.0)	6.7(3.1,17.0)

■ **Six patients in the ASC22 group achieved HBsAg loss at week 24 (Figure 2).**

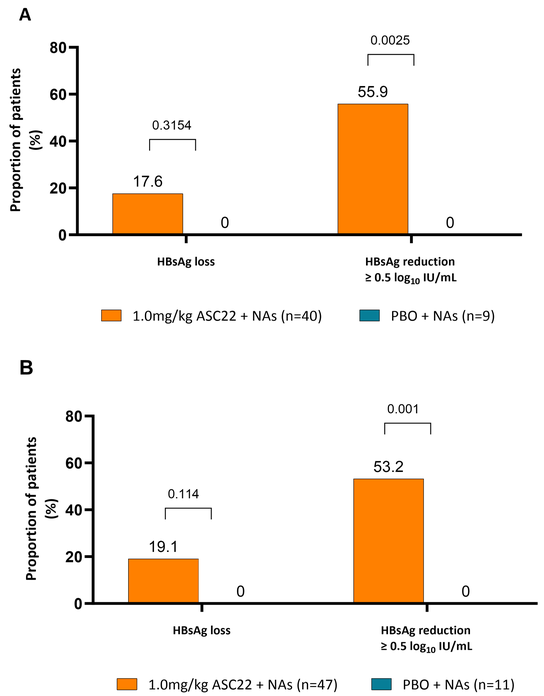


Figure 2. HBsAg Change from baseline

The proportion of HBsAg responders at week 24 in the extension cohort, stratified by HBsAg loss and reduction(Panel A). In the ASC22 group, HBsAg loss and reduction ≥ 0.5 log were observed in 6 patients (17.6%) and 19 patients (55.9%), respectively, compared to 0 in the placebo group.

The proportion of HBsAg responders at week 24 in patients with baseline HBsAg ≤100 IU/mL was assessed in a subgroup analysis across the entire study, including the extension cohort and 1.0 mg/kg cohort(Panel B). In the ASC22 group, 9 patients (19.1%) showed HBsAg loss and 25 patients (53.2%) showed a reduction of HBsAg ≥ 0.5 log, while 0 in the placebo group.

■ **Patients with ALT or AST flares experienced a more significant decline in HBsAg levels (Table 2).**

Table 2. HBsAg response in patients with ALT or AST flare.

	ASC22 + NAs (n=40)	PBO (n=9)
ALT Flare, n(%)	5(12.5%)	0(0.0%)
AST Flare, n(%)	4(10.0%)	0(0.0%)
HBsAg reduction in the patient with ALT flare, log$_{10}$ IU/mL(Mean)	-1.5	0.0
HBsAg reduction in the patient with AST flare, log$_{10}$ IU/mL(Mean)	-1.6	0.0

ALT or AST flare was defined as a transient rise of ALT or AST >2 × ULN and >3 × BL level.

■ **ASC22 combined with NAs treatment showed acceptable safety and tolerability over 24 weeks.**

Table 3. Safety Summary

Event, n(%)	1.0mg/kg ASC22 + NAs (n=100)	PBO+NAs (n=39)
All AE	94(94)	35 (89.7)
AE attributed to ASC22 or PBO	76(76)	2 (5.1)
Grade 1-2	69(69)	2 (5.1)
Grade 3	7(7)	0
SAE[a]	1(1)	0
AE leading to withdraw	7(7)	0
Death	0	0
AEs with a drug-related incidence > 10%		
ALT elevation	30(30)	1 (2.6)
AST elevation	23(23)	0
rash	17(17)	0
Allergic dermatitis	12(12)	0
Endocrine system diseases	12(12)	0

AE: Adverse event; SAE: Serious adverse event. a: One patient experienced acute urticarial. A pooled safety analysis was conducted for all patients who received at least one dose of 1.0 mg/kg ASC22 after enrollment, including those in the expansion cohort(Table 3).

Conclusion

ASC22 monotherapy with background NAs showed statistically significant HBsAg reduction and 6(17.6%) HBsAg loss after 24-week treatment. Together with the acceptable safety profile and convenient subcutaneous injections, ASC22 demonstrated potential as a promising immune-therapy for CHB with low BL HBsAg levels.

Disclosures

This study was sponsored by Ascletis BioScience. Ascletis BioScience was involved with the study design, statistical analysis, interpretation of data, decision to publish, and preparation of the abstract and poster. Y. Y., and J.J.W. are employees and stock/shareholders of Ascletis BioScience. The remaining authors declare no competing interests.