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HBsAg Loss in Chronic Hepatitis B Patients After 24-Week Treatment with Subcutaneously Administered PD-L1 Antibody ASC22 (Envafolimab): Interim Results from a Phase IIb Extension Cohort

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Background

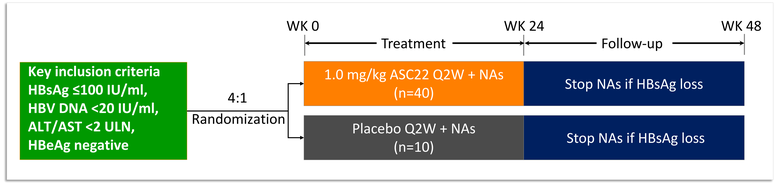
Data from the previously completed Phase IIb study indicated that in 1.0 mg/kg ASC22 Q2W cohort (n=48, per protocol), more HBsAg reduction was observed in chronic hepatitis B (CHB) patients with lower baseline HBsAg. Among 48 patients, 7 of them had baseline HBsAg ≤ 100 IU/mL and 3 patients (3/7, 42.9%) achieved sustained HBsAg loss (< 0.05 IU/mL) after 24-week treatment and 24-week follow-up, indicating functional cure. Building upon this promising outcome, we initiated an extension cohort of patients with baseline HBsAg ≤100 IU/ml to explore sustained HBsAg loss in this specific population.

Methods

This randomized, single-blind, multi-center, phase IIb extension cohort study design is shown in Figure 1.

- The primary efficacy endpoint is HBsAg reduction. If HBsAg loss at week 24, stop NAs during the follow-up. Otherwise continue NAs during the follow-up.
- Interim analysis was conducted when approximately 50% of enrolled patients completed 24-week treatment of ASC22 or placebo.

Figure 1: Study design



Results

ASC22 expansion cohort enrolled 49 patients. 25 patients completed 24-week treatment (19 in ASC22 cohort and 6 in placebo cohort). Here we report the efficacy and safety in patients who completed 24-week treatment.

- **Baseline characteristics between ASC22 and PBO groups were comparable. (Table 1.)**
- **In ASC22 cohort at week 24, 4 (21.1%) patients achieved HBsAg loss (< 0.05 IU/ml) (Table 2). Figure 2 depicts changes in HBsAg, ALT and cytokines over 24 weeks in a patient achieved HBsAg loss.**

Results

- **ALT or AST flares (defined as ALT/AST >2X ULN and >3X baseline level) were observed in ASC22 cohort (2/19) only, which were associated with more significant HBsAg reduction from baseline (-1.86 log_{10} IU/mL).**
- **ASC22 was generally safe and well tolerated. Safety results are presented in Table 3. During 24-week treatment, 3 patients (3/19, 15.8%) experienced thyroid dysfunction related AEs (grade 1 only).**

Table 1. Baseline characteristics and demographics

Characteristics	1.0mg/kg ASC22+NAs (N=19)	PBO+NAs (N=6)
Male, n(%)	15 (78.9%)	5 (83.3%)
Age, Median(range)	46(27, 60)	50(34, 60)
BMI (kg/m^2), Mean(SD)	23.5 (2.5)	24.3 (2.1)
ALT (IU/L), Mean(SD)	21.6 (8.7)	27.0 (15.7)
AST (IU/L), Mean(SD)	23.5 (5.4)	23.2 (2.0)
HBsAg(IU/L), Mean(SD)	32.8(33.3)	26.3(27.5)

Table 2. Changes in HBsAg from baseline at the end of treatment (week 24)

	1.0mg/kg ASC22+NAs (n=19)	PBO+NAs (n=6)
HBsAg loss, n(%)	4(21.1%)	0
HBsAg reduction ≥1 log_{10} IU/mL, n(%)	8(42.1%)	0
HBsAg reduction ≥0.5 log_{10} IU/mL, n(%)	11(57.9%)	0
HBsAg reduction ≥0.3 log_{10} IU/mL, n(%)	12(63.2%)	1(16.7%)

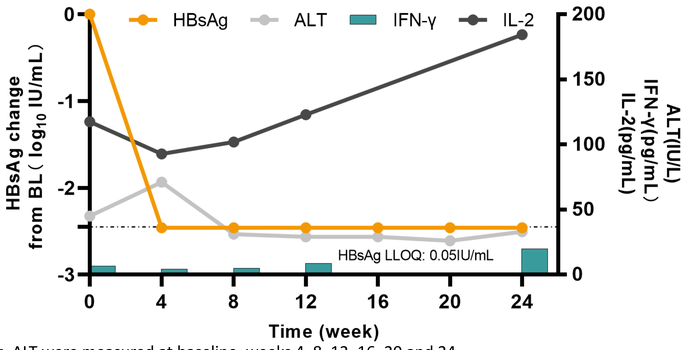
Table 3. On-treatment safety results

	1.0mg/kg ASC22+NAs (N=19)	PBO+NAs (N=6)
	n (%)	n (%)
All AEs	18 (94.7)	6 (100.0)
Grade ≥3 AEs	2 (10.5)	0 (0.0)
AEs related to experimental drugs	17 (89.5)	0 (0.0)
Grade ≥3 AEs[a]	1 (5.3)	0
leading to discontinuation	2 (10.5)	0
leading to early withdrawal	0	0
leading to death	0	0
SAE[b]	1 (5.3)	0 (0.0)

a: One patient with HBsAg loss experienced a grade 3 ALT and AST elevation.

b: One Grade 3 SAE of coronary atherosclerotic heart disease was considered as possibly unrelated to ASC22.

Figure 2. Clinical measures of a patient who achieved HBsAg loss



HBsAg, ALT were measured at baseline, weeks 4, 8, 12, 16, 20 and 24.
INF-γ and IL-2 were measured at baseline, weeks 4, 8, 12 and 24.

Conclusions

- **ASC22 monotherapy with background NAs showed statistically significant HBsAg reduction and 21.1% (4/19) 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.**