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HBsAg Loss in Chronic Hepatitis B Patients with Subcutaneous PD-L1 Antibody ASC22 (Envafolimab) plus Nucleos(t)ide Analogs Treatment: Interim Results from a Phase IIb Clinical Trial

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Disclosure

Conflict of Interest Disclosure Statement

Dr. Jinzi J. Wu is CEO of Ascletis.

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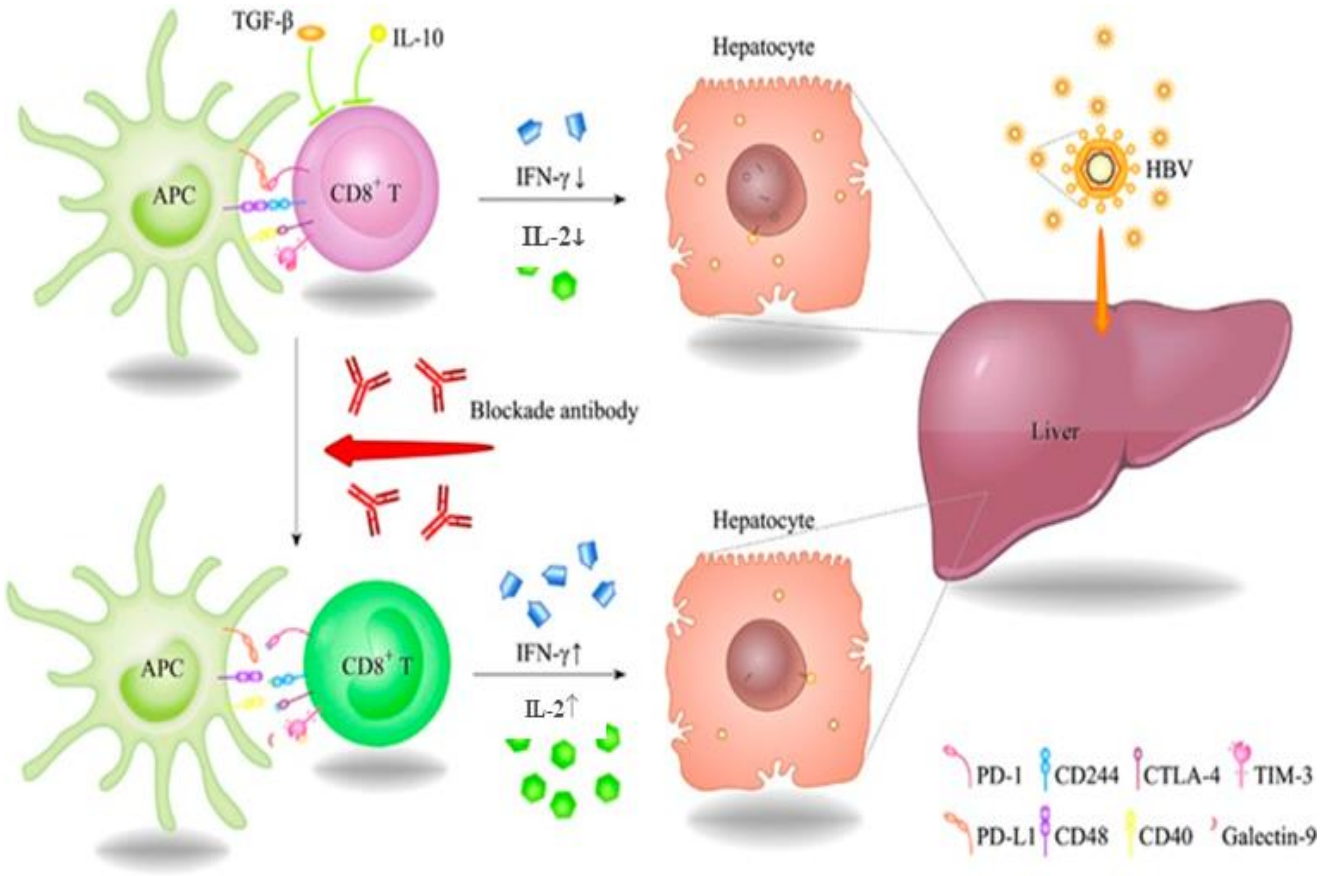
PD-L1 and Chronic Hepatitis B (CHB)



PD-1/PD-L1 interaction leads to

T cell exhaustion

—— **Persistent HBV infection**

Blockade of PD-1/PD-L1

pathway restores T cell function

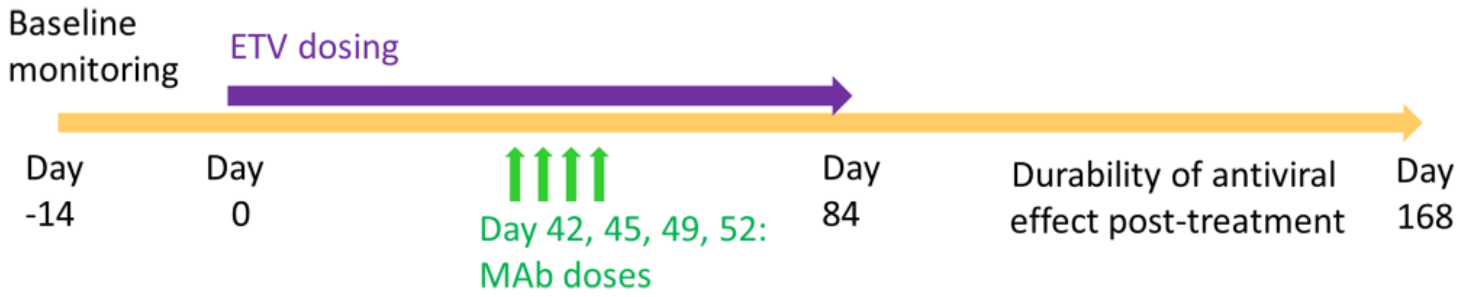
—— **Elimination of HBV**

1. Mol Immunol. 2008;45(4):963-70.
2. Cell Death Dis. 2015 Mar 19;6:e1694.

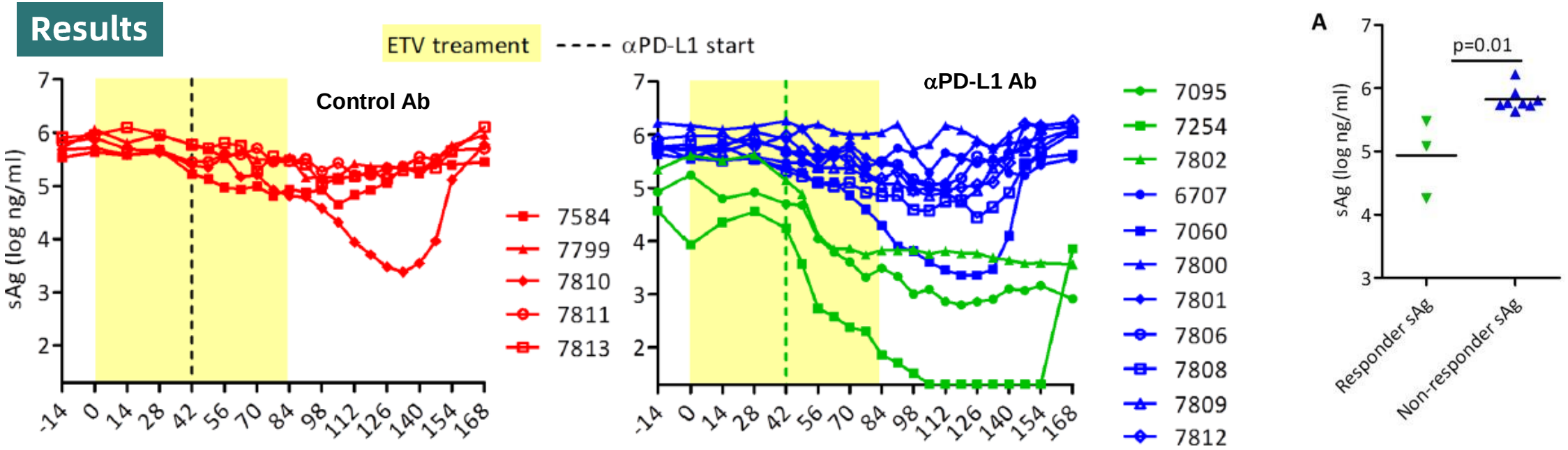
- **Combining PD1/PD-L1 inhibitor drug with nucleos(t)ide analogue or other anti-viral treatment may be a cure for CHB.**

PD-L1 antibody study in woodchuck hepatitis virus (WHV) model

Design



Results



- **Combining αPD-L1 Ab with ETV can induce reduction of sAg in WHV model, especially for animals with a lower pre-treatment sAg level.**

Balsitis, S., et al., PLoS One, 2018, 13(2): e0190058.

Envafolimab (ASC22), an anti-PD-L1 antibody

- A humanized single-domain PD-L1 antibody fused with human IgG1 Fc.
- **A BLA submitted for oncology indication with large safety data**.

- Compared to conventional PD-L1 antibodies,

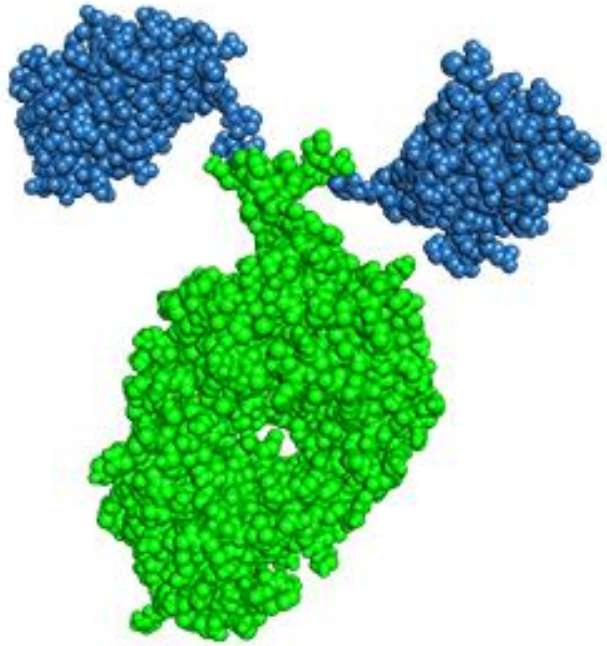
  ASC22's unique competitive profile includes:

  - half-size of conventional PD-L1 Ab

  - subcutaneously injectable

  - high affinity and room temp stability

  - low immunogenicity

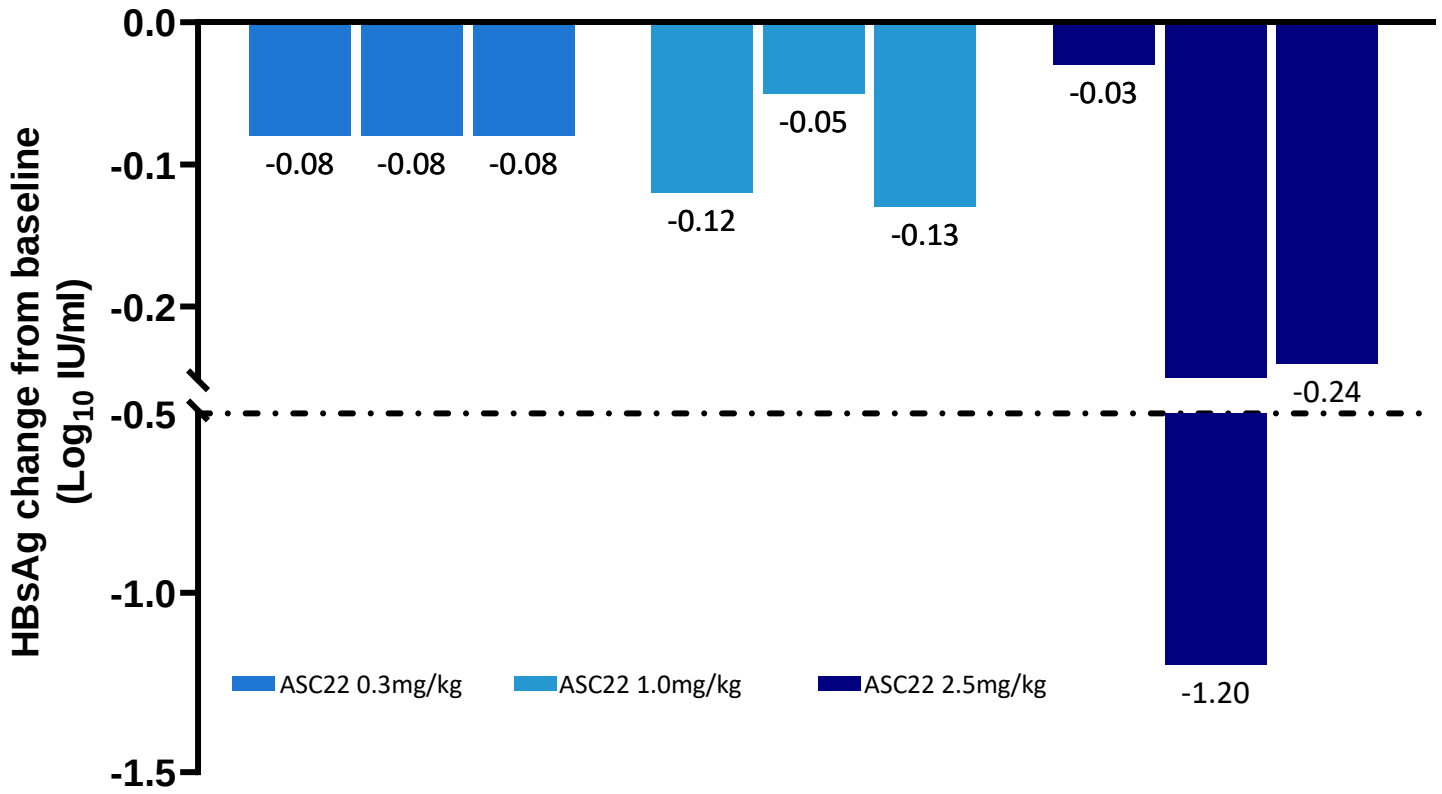


ASC22, also known as KN035:
Crystal Structure

http://www.alphamabonc.com/en/pipeline/kn035.html

ASC22 Phase IIa Single Dose Escalation: HBsAg Reduction is Dose Dependent

Maximum HBsAg Reduction During 12-Week Follow-up After Single Dose

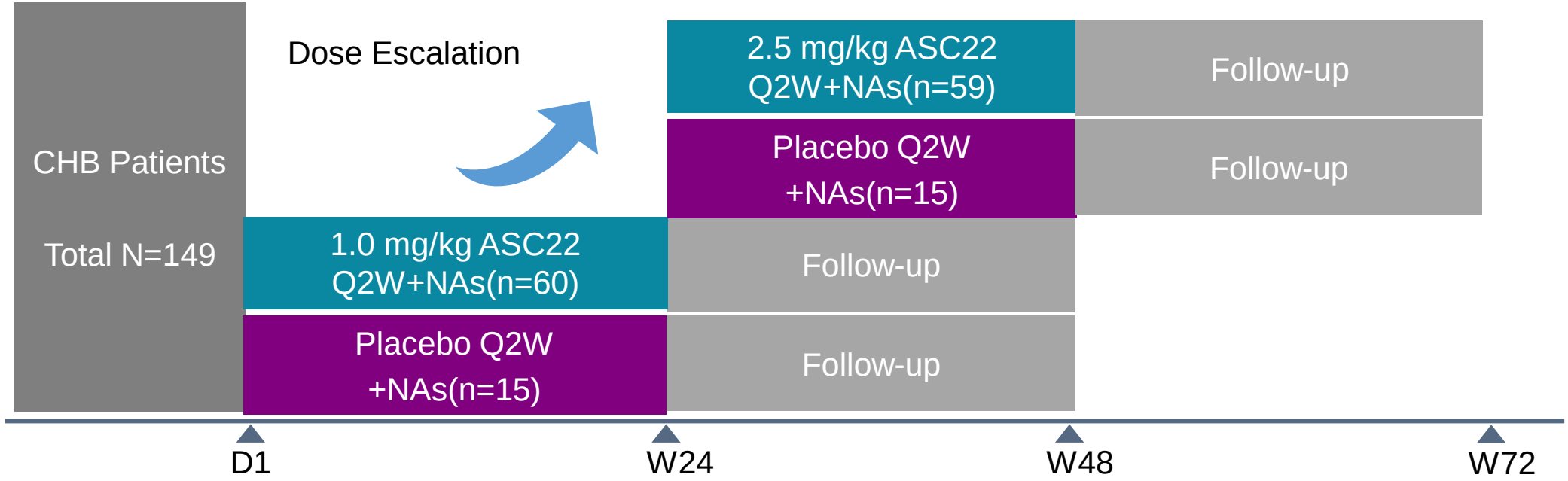


Among 3 patients receiving 2.5 mg/kg dose, 1 patient achieved a maximum HBsAg reduction of 1.2 $\log_{10}$ IU/mL.

ASC22 Phase IIb clinical trial (NCT04465890)

Study design:

- A randomized, single-blind, multi-center Phase IIb trial
- Inclusion criteria: HBsAg ≤ 10,000 IU/mL, HBV DNA < 20 IU/mL, ALT/AST < 2 ULN, negative HBeAg.



Aim:

To assess efficacy and safety of ASC22 of 24-week treatment and 24-week follow-up in CHB patients

Interim Report of ASC22 Phase IIb Clinical Trial

Based on the 44 patients who completed 24-week treatment.

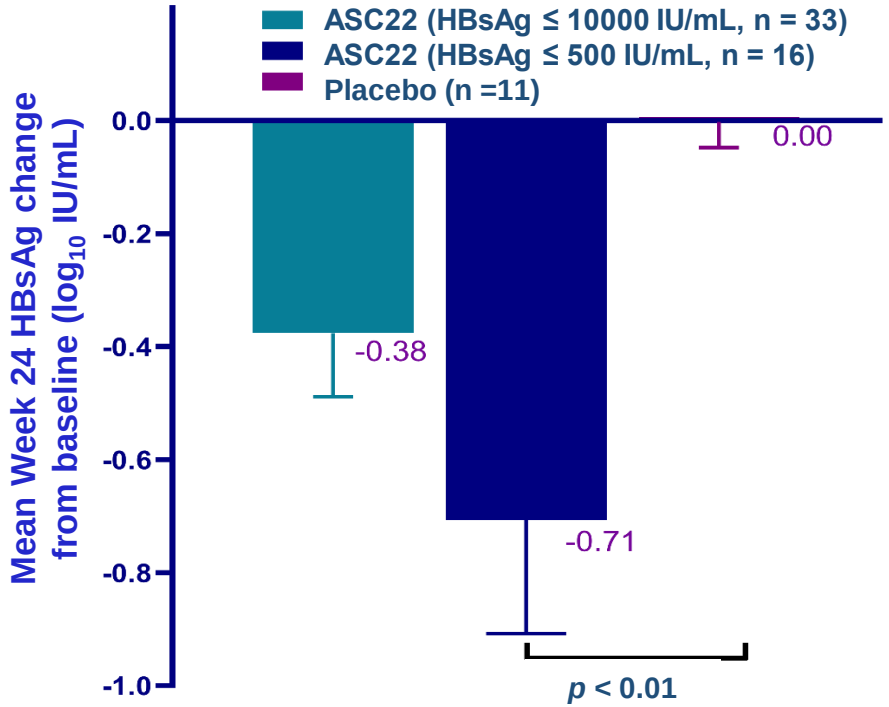
- **1 mg/kg ASC22 + Nucleos(t)ide Analogs (NAs): n = 33**
- **Placebo (PBO) + NAs: n = 11**

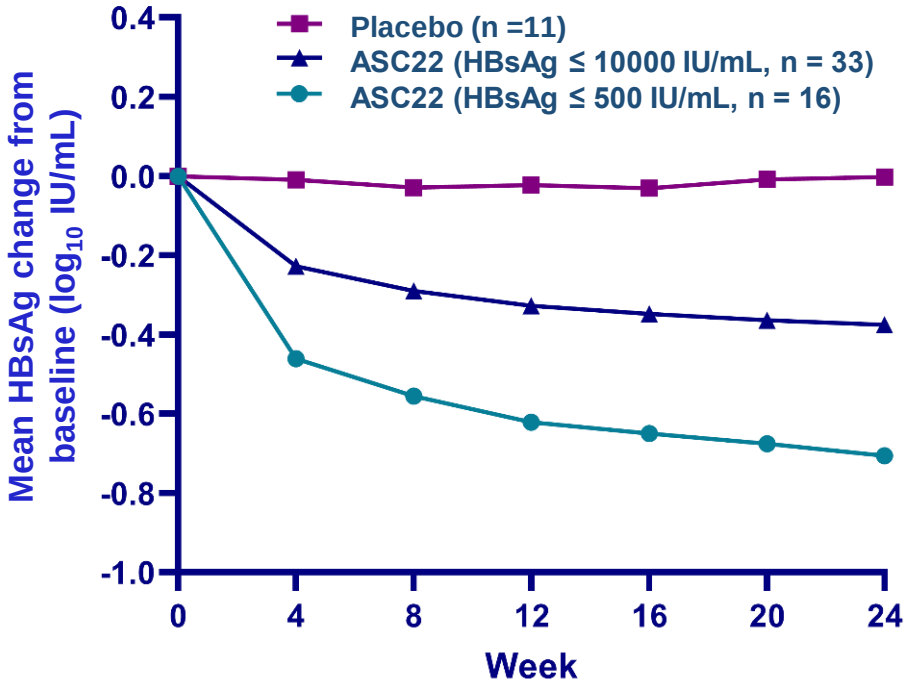
Demographic and Baseline Characteristics

	ASC22 1.0mg/kg (n = 33)	Placebo (n = 11)
Median age, yrs (range)	38(23 ~ 59)	41(33 ~ 48)
Male, n (%)	24(73%)	9(82%)
Chinese,n(%)	33(100%)	11(100%)
Median BMI, kg/m^2 (range)	23(18 ~ 28)	24(20 ~ 28)
Median HBsAg, log_{10}IU/mL (range)	2.7 (0.2~3.7)	2.7 (1.0~3.5)
HBsAg ≤ 500 IU/mL, n (%)	16(48%)	4(36%)
HBeAg negative, n (%)	33(100%)	11(100%)
Median ALT, U/L (range)	23.0(10.0~65.0)	19.0(8.0-55.0)
Median AST, U/L (range)	23.0(16.9~64.0)	22.0(14.0~31.0)

- **Baseline characteristics between ASC22 and PBO groups are comparable.**

ASC22 plus NAs treatment can induce HBsAg reduction





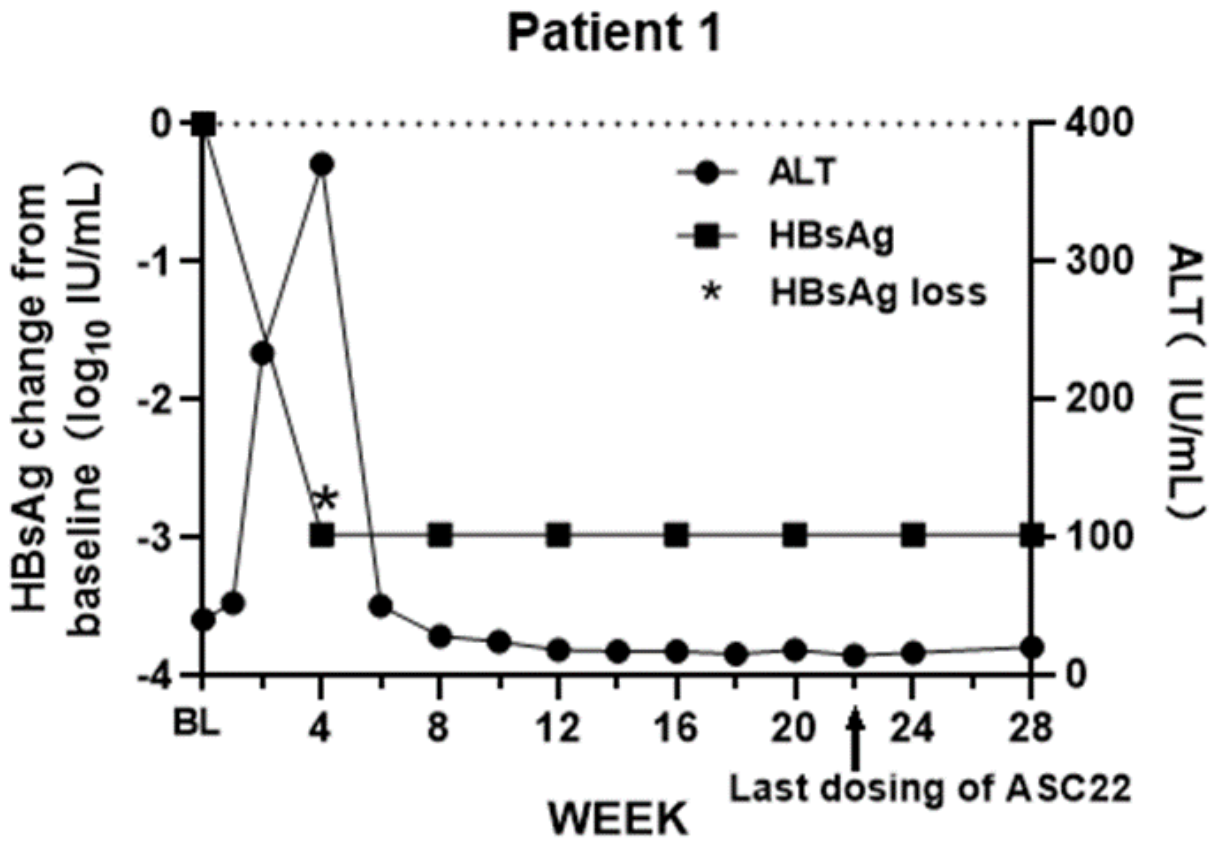
- ASC22 can induce HBsAg reduction, especially for patients with baseline HBsAg ≤ 500 IU/mL

ASC22 can even induce HBsAg loss

Outcomes after 24 weeks treatment of ASC22	Baseline HBsAg ≤ 10000 IU/mL (N =33)	PBO + NAs (N = 11)	*P* value
Mean HBsAg change frpm baseline (log_{10} IU/mL)	-0.38	0	0.0639
HBsAg reduction ≥ 0.5 log_{10} IU/mL	7 (21%)	0 (0%)	-
HBsAg Loss	*3 (9%)*	*0 (0%)*	-
Outcomes after 24 weeks treatment of ASC22	**Baseline HBsAg ≤ 500 IU/mL (N =16)**	**PBO + NAs (N = 11)**	***P* value**
Mean HBsAg change frpm baseline (log_{10} IU/mL)	-0.7	0	**0.0084**
HBsAg reduction ≥ 0.5 log_{10} IU/mL	7 (44%)	0 (0%)	-
HBsAg Loss	*3 (19%)*	*0 (0%)*	-

- **7 patients in ASC22 group compared to none in PBO group achieved HBsAg reduction ≥ 0.5 log_{10} IU/mL.**
- **3 patients obtained HBsAg loss (undetectable, < 0.05 IU/mL) at Week 4, 16 and 16, respectively,**

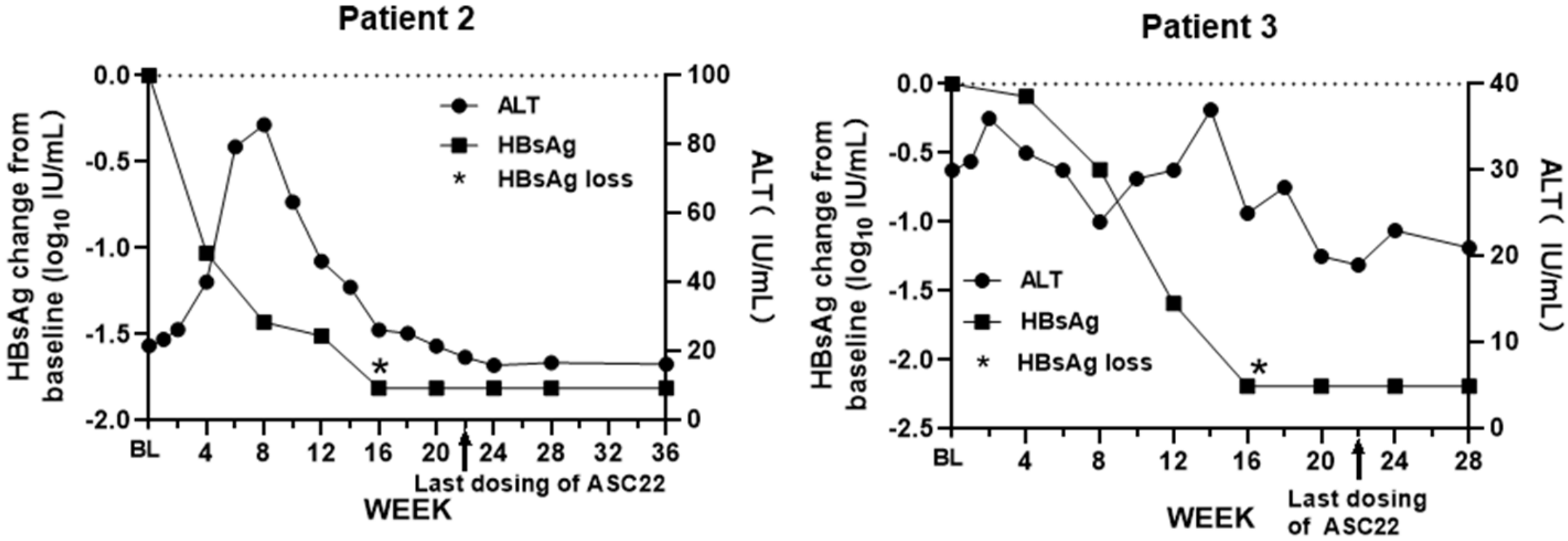
HBsAg loss was accompanied with an ALT flare



- **ALT flares were observed in 4/7 (57%) and 2/3 (67%) patients with HBsAg reduction ≥ 0.5 log_{10} IU/mL and HBsAg loss (undetectable, < 0.05 IU/mL), respectively.**

"*" indicates onset of HBsAg loss

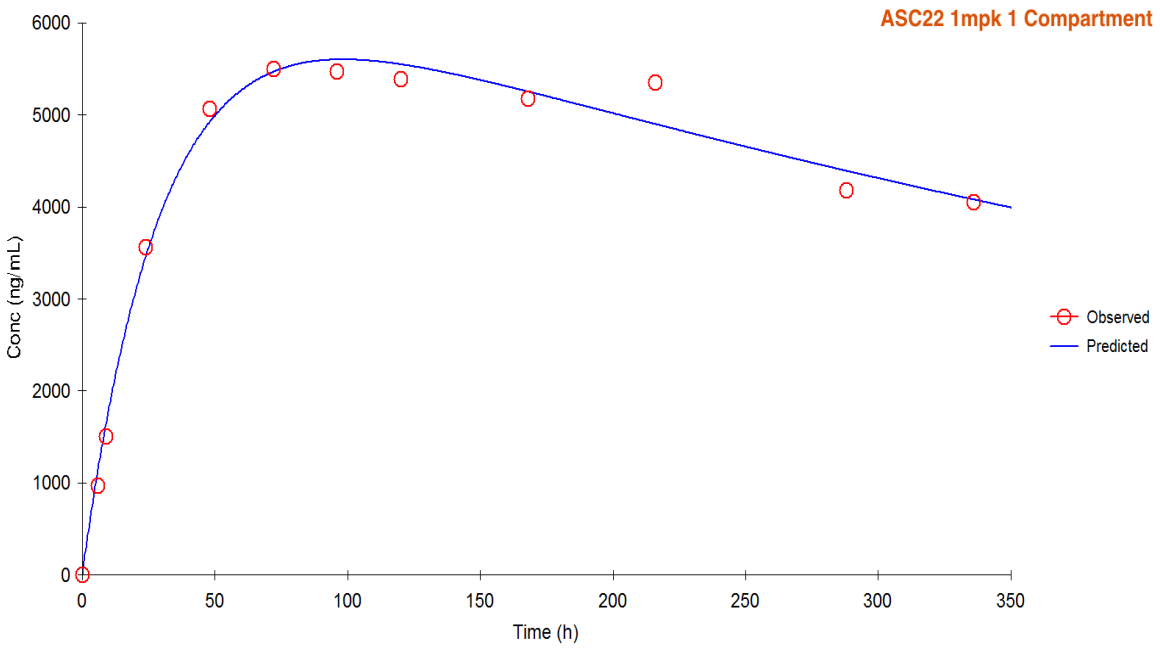
HBsAg seroclearance maintained up to14 weeks after last dosing of ASC22



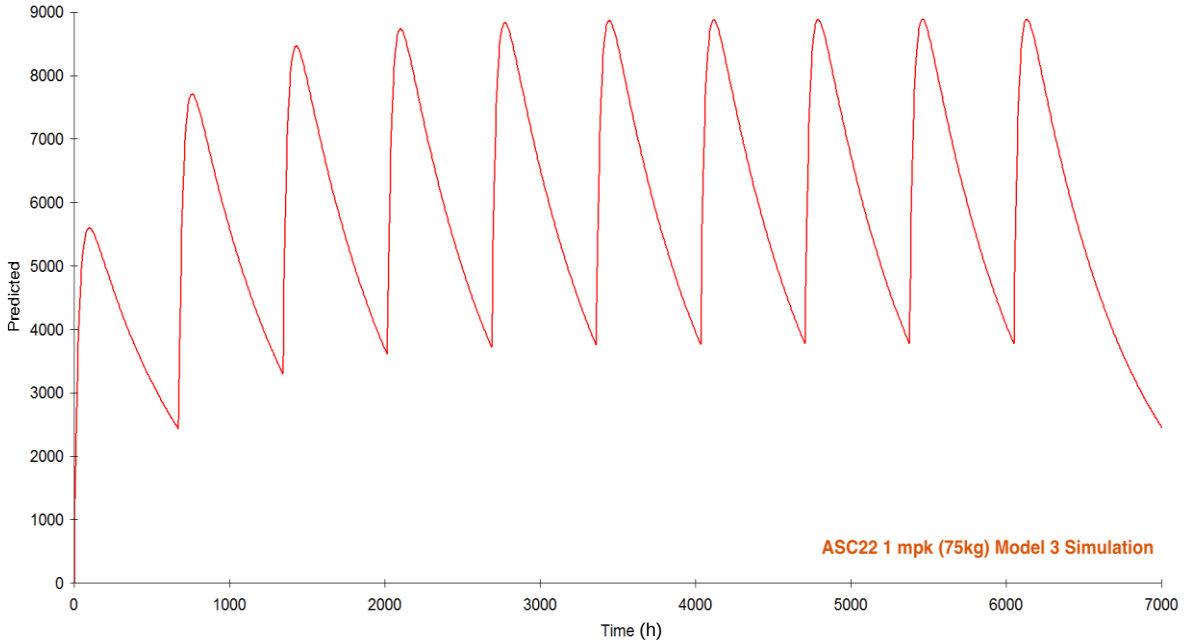
- All three patients who obtained HBsAg loss during ASC22 treatment still maintained HBsAg undetectable (< 0.05 IU/mL) 6-14 weeks after last dosing of ASC22.

The predicted C_{min} of 1 mg/kg ASC22 at Steady State One month after dosing

The observed PK profile (1 mg/kg on Day 1)



The predicted PK profile (Q4W, 1 mg/kg)



Predicted C_{min} (Q4W) at steady state = 3778 ng/mL

- **Predicted C_{min} value of ASC22 at steady state is > 3000 ng/mL one month after dosing, indicating > 90% receptor occupancy and ASC22 has the potential to be given once monthly.**

Summary of ASC22 Phase IIb Study

- In CHB patients with baseline HBsAg ≤ 500 IU/mL, 24-week treatment of ASC22 Q2W plus NAs resulted in 19% patients with HBsAg seroclearance.
- Subcutaneous administration of ASC22 Q2W plus NAs for 24 weeks is shown to be safe and well-tolerated.
- PK data showed that C_{min} value of ASC22 at steady state was predicted to be > 3000 ng/mL one month after dosing, indicating > 90% receptor occupancy and ASC22 has the potential to be given once monthly.

Thank You

On behalf of all ASC22 investigators and their teams, thanks to our patients and their families.

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