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A Phase IIa trial of Subcutaneously Administered PD-L1 Antibody ASC22 (Envafolimab) in Patients with Chronic Hepatitis B

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Disclosure

Conflict of Interest Disclosure Statement

I, Guiqiang Wang, received research fund from Ascletis and serve as a consultant or advisory board member for Abbott, AbbVie, Bristol-Myers Squibb, Gilead Sciences, Janssen, and Roche.

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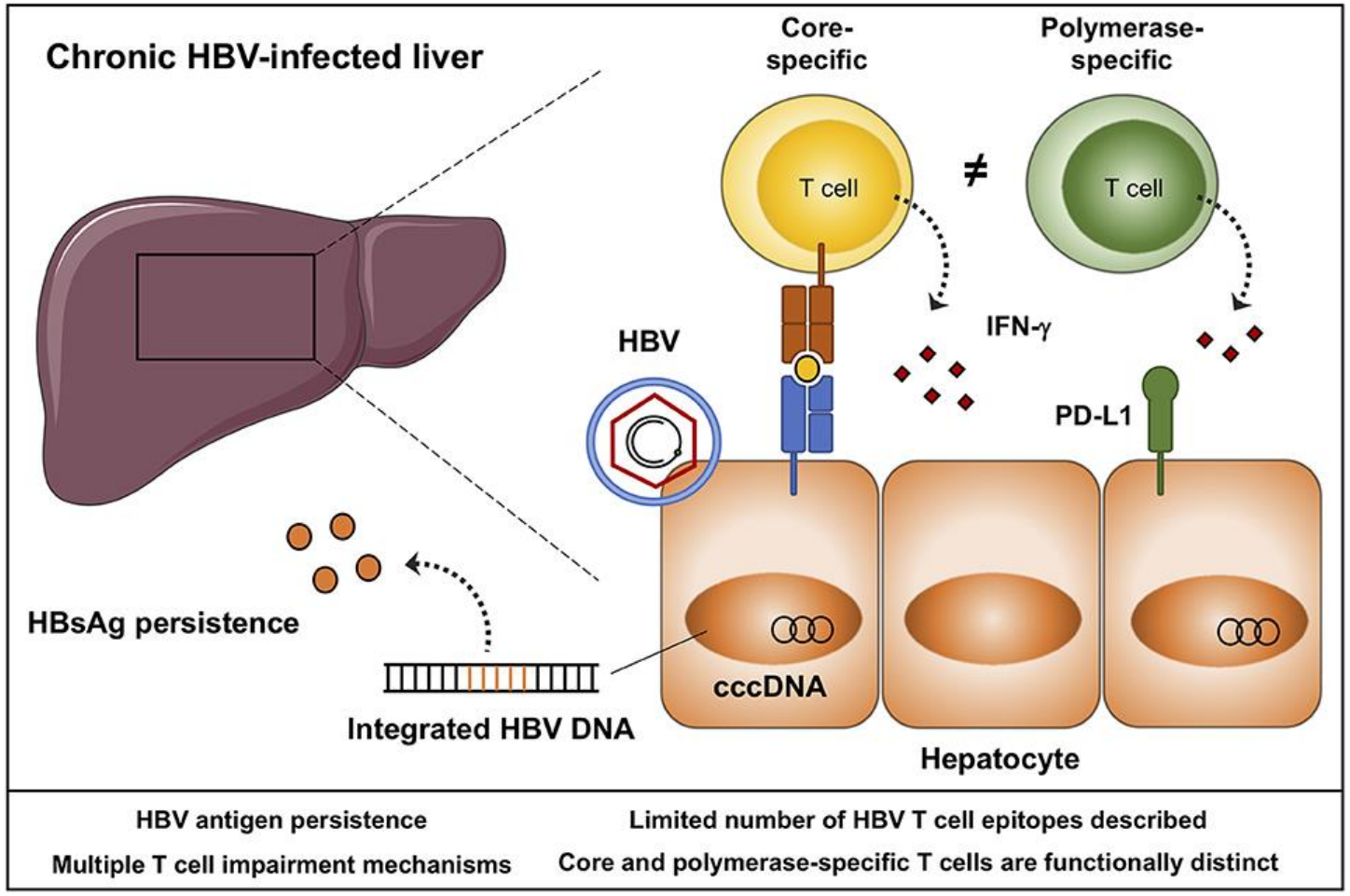
Background of Chronic Hepatitis B (CHB)

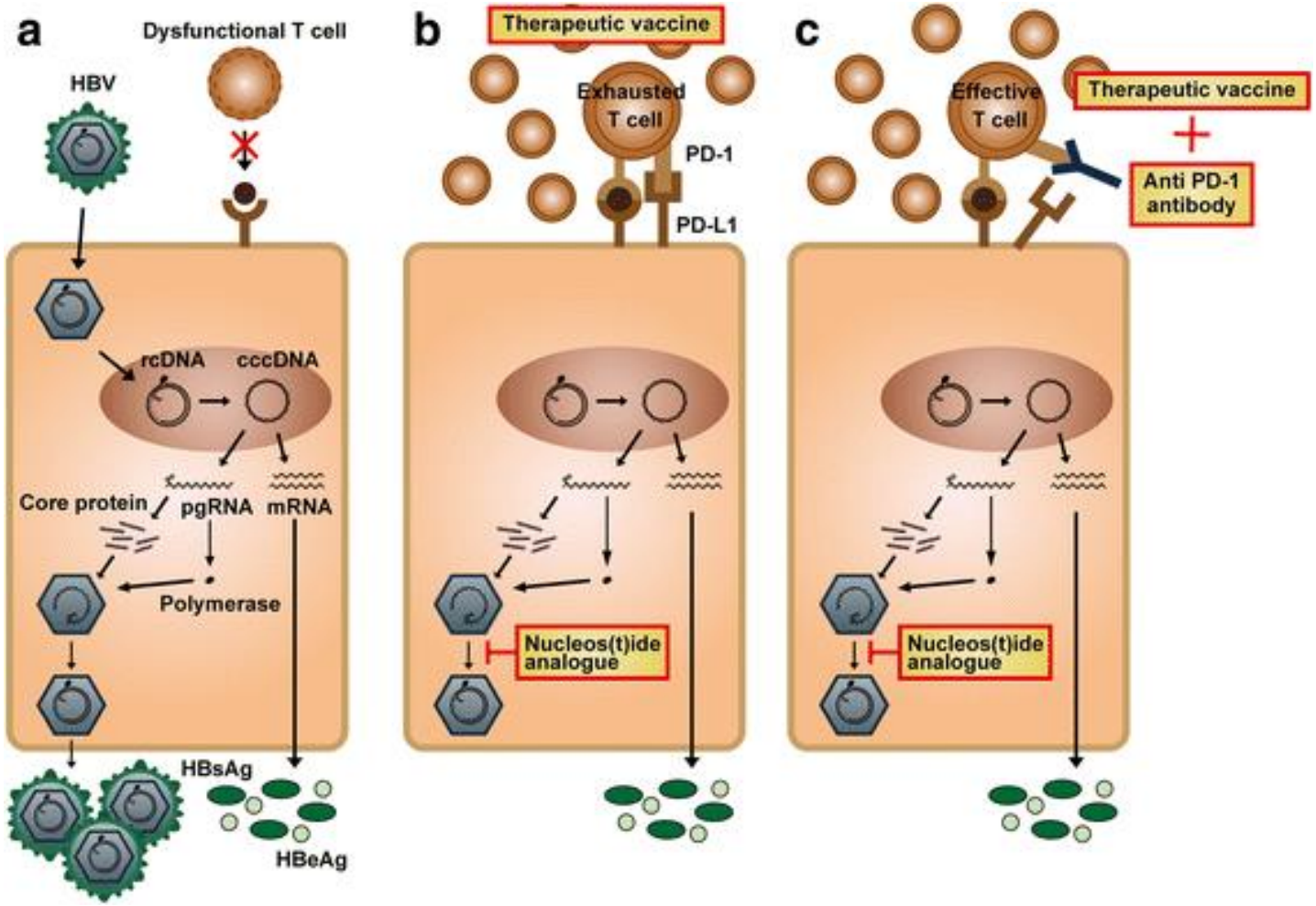


Hoogeveen, R. C.; Boonstra, A., Frontiers in immunology, 2020, 11:401.

- An insufficient T-cell response to HBV antigen is characteristic of CHB and limits durable viral control and clearance.
- T-cell exhaustion is a major pathway mediating impaired *in situ* response.
- Dysfunctional T-cells have more PD-1 expression.

Blockade of PD-1/PD-L1 pathway might be a cure for CHB

- Blockade of PD-1/PD-L1 pathway can restore T Cell immune function.
- Combining anti-PD1/anti-PD-L1 drug with nucleos(t)ide analogue or other anti-viral treatment may be a solution to cure CHB.



Tseng, T. C.; Kao, J. H., BMC Med, 2017, 15(1): 53.

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,

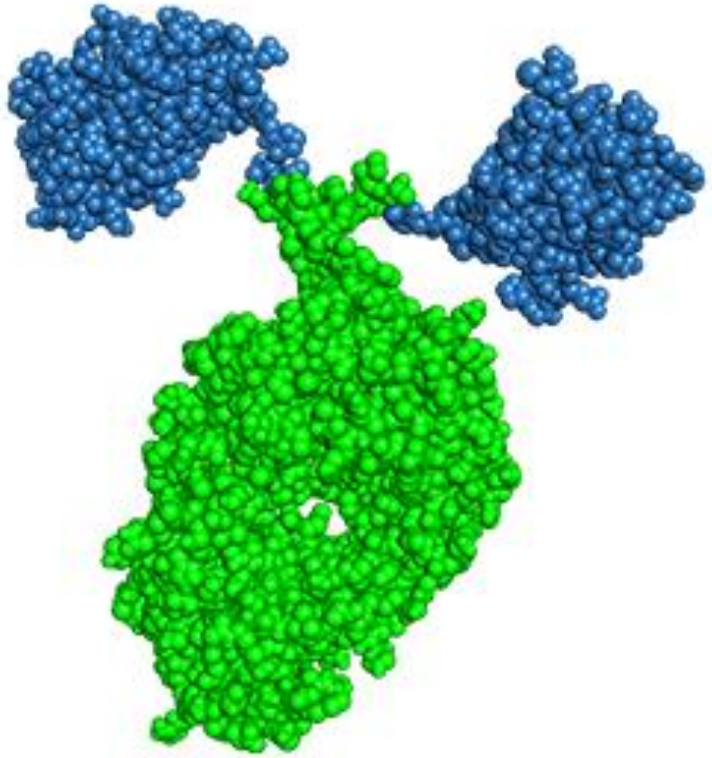
  ASC22's unique competitive profile includes:

  - 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 Study Design (NCT04465890)

Aim: Efficacy and safety assessment of ASC22 in single dose.

single dose
subcutaneous injection of ASC22

Enrollment

NAs experienced patients
(n = 9)
- HBV DNA < 20 IU/mL
- HBeAg negative
- HBsAg < 10000IU/mL
- Non cirrhosis
- AST、ALT ≤ 2 × ULN

Cohort 1: ASC22 0.3mg/kg (n=3)	Continue NAs treatment
Cohort 2: ASC22 1.0mg/kg (n=3)	Continue NAs treatment
Cohort 3: ASC22 2.5mg/kg (n=3)	Continue NAs treatment

- Week 4 — Week 0 — follow-up — Week 12

Primary endpoint

Efficacy: HBsAg change from the baseline

Safety: Adverse events reported

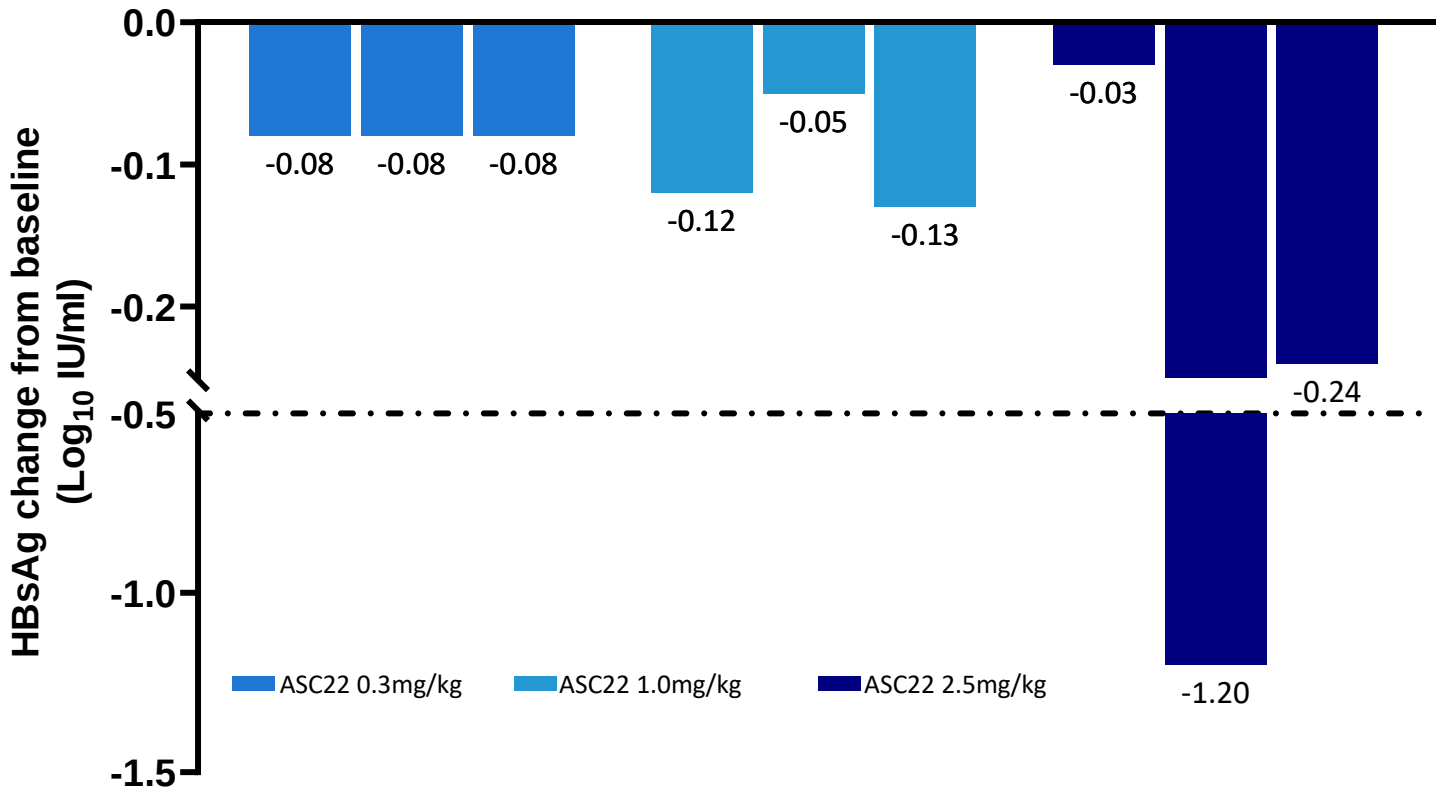
Demographic and Baseline Characteristics

	ASC22 0.3mg/kg (n=3)	ASC22 1.0mg/kg (n=3)	ASC22 2.5mg/kg (n=3)
Median age, yrs (range)	31(30-42)	29(27-33)	38(37-52)
Male, n (%)	2(67%)	1(33%)	1(33%)
Asian,n (%)	3(100%)	3(100%)	3(100%)
Median BMI, kg/m^2 (range)	25(21-26)	25(24-25)	24(22-25)
Median HBsAg, log10IU/mL (range)	3.4(2.7-3.8)	3.5(2.9-3.9)	2.9(2.2-3.0)
HBsAg >1,000 IU/mL, n (%)	2(67%)	2(67%)	1(33%)
HBeAg negative, n (%)	3(100%)	3(100%)	3(100%)
Median ALT, U/L (range)	26(12-27)	17(11-25)	11(9-13)
Median AST, U/L (range)	23(19-24)	18(17-23)	16(14-18)
Oral HBV therapy, n (%)			
TDF	3(100%)	2(67%)	1(33%)
ADV	1(33%)		
ETV		1(33%)	2(67%)
LDT		1(33%)	1(33%)

- Baseline HBsAg levels were comparable.

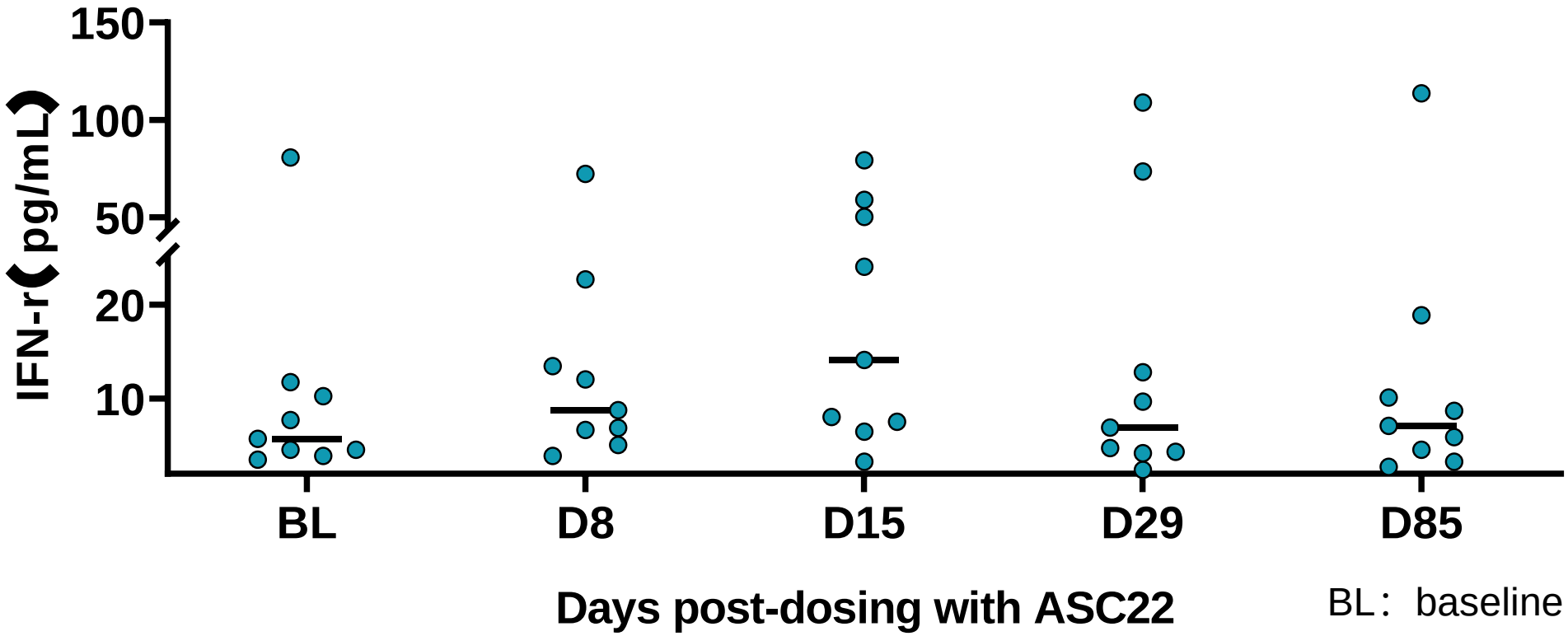
HBsAg Reduction is ASC22 Dose Dependent

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



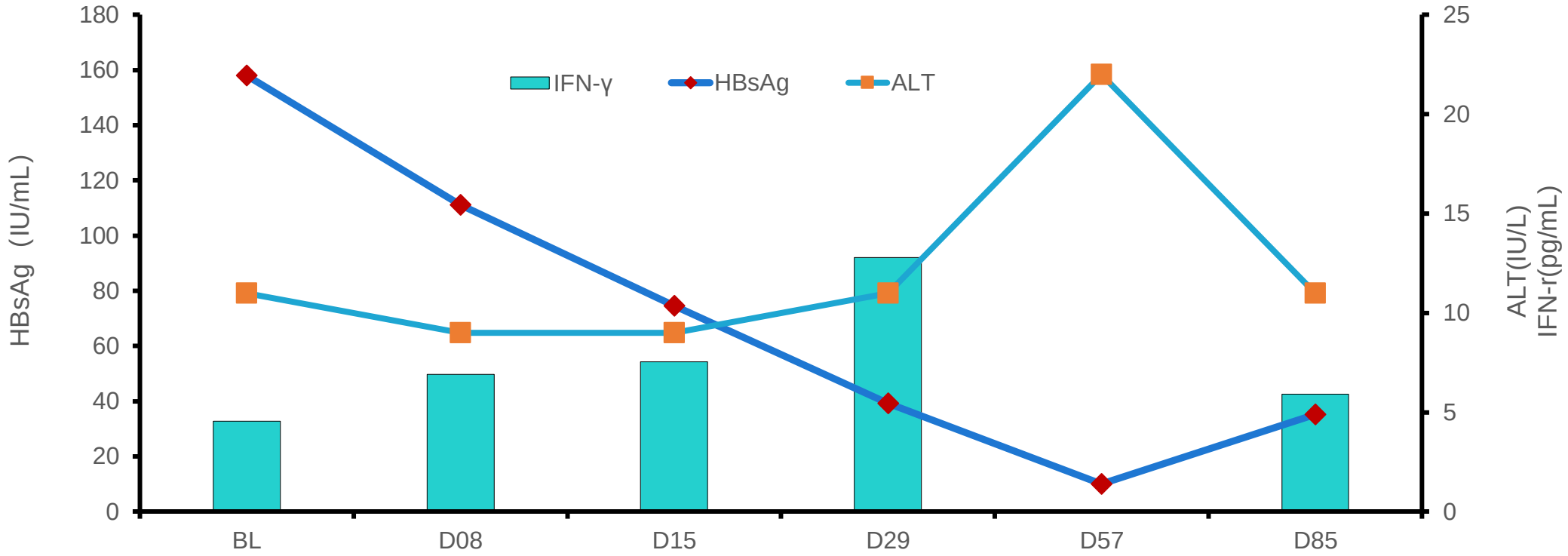
Among 3 patients receiving 2.5 mg/kg dose, 1 patient achieved a maximum HBsAg reduction of 1.2 $\log_{10}$ IU/mL.

Monitoring of IFN-γ Responses during Follow-up



- IFN-γ was increasing after ASC22 treatment and peaked around Day 15.

Comparison of serum HBsAg, IFN-γ and ALT Level during Follow-up in One Patient



BL：baseline； IFN-γ was not measured on Day 57

- An ALT flare was observed on Day 57 when HBsAg reached maximum reduction.
- HBsAg reduction was accompanied by elevation of IFN-γ.

Safety Profile of ASC22 During Follow-up

n (%)		ASC22 0.3mg/kg (n=3)	ASC22 1.0mg/kg (n=3)	ASC22 2.5mg/kg (n=3)
Overall Safety	Any AE	3 (100)	3 (100)	3 (100)
	Any Grade 3/4	0 (0)	0 (0)	0 (0)
	ASC22 related AE	0 (0)	0 (0)	0 (0)
	SAE	0 (0)	0 (0)	0 (0)
	Death	0 (0)	0 (0)	0 (0)
Grade 3/4 Lab Abnormalities	Thrombocytopenia	0 (0)	0 (0)	0 (0)
	Leukopenia	0 (0)	0 (0)	0 (0)
	Neutropenia	0 (0)	0 (0)	0 (0)
	ALT/AST	0 (0)	0 (0)	0 (0)

- All AEs were grade 1.
- No Grade ≥ 2 AE occurred.
- No premature withdrawal or death.

Summary of ASC22 Phase IIa Study

- Single subcutaneous dose ASC22 (Envafolimab) induced a does-dependent reduction of HBsAg.
- Single subcutaneous dose ASC22 up to 2.5 mg/kg is safe and well-tolerated.
- IFN-γ was increasing after single subcutaneous dose ASC22 treatment.
- ASC22 has potential to cure CHB patients in combination with other therapies.
- Based on the positive results from this Phase IIa trial, ASC22 Phase IIb trial (24-week treatment of ASC22, Q2W plus NAs) has been initiated.

Thank You

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

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