Taipei APASL 2023

ANNUAL MEETING

Innovation and Paradigm Shift in Hepatology

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Effects of Subcutaneous PD-L1 Antibody ASC22 (Envafolimab) Plus nucleos(t)ide analogs on HBsAg reduction in patients with chronic hepatitis B infection are correlated with pre-treatment HBsAg level

Guiqiang Wang[1], Yimin Cui[1], Yao Xie[2], Qianguo Mao[3], Qing Xie[4], Ye Gu[5], Xinyue Chen[6], Guoxin Hu[7], Yongfeng Yang[8], Handan He[9], Jinzi J.Wu[9]

Presenting author： Guiqiang Wang，Peking University First Hospital

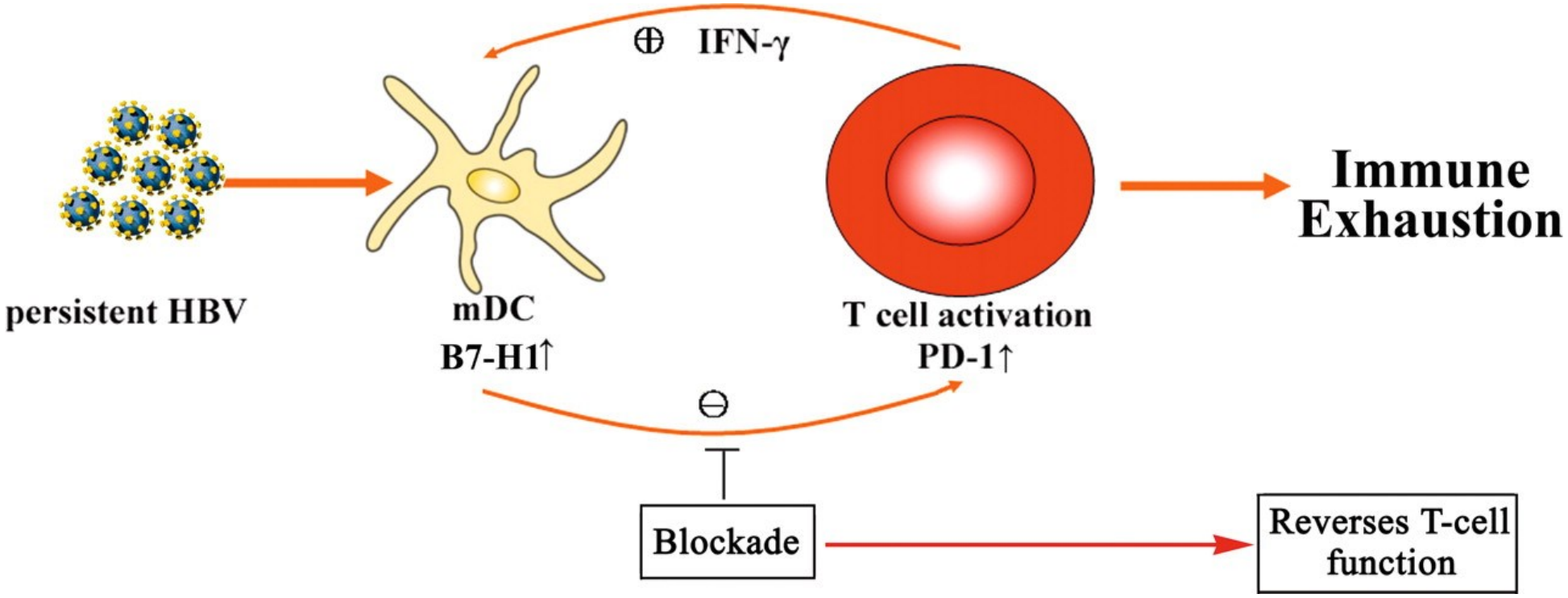
Disclosure

Conflict of Interest Disclosure Statement

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

Guiqiang Wang, M.D.,
Director, Department of Infectious Disease,
Director, Center for Liver Disease, Peking University First Hospital,
Director, Department of Infectious Disease, Peking University International Hospital,
E-mail: john131212@126.com
Web: https://www.pkufh.com/Html/Doctors/Main/Index_1129.html

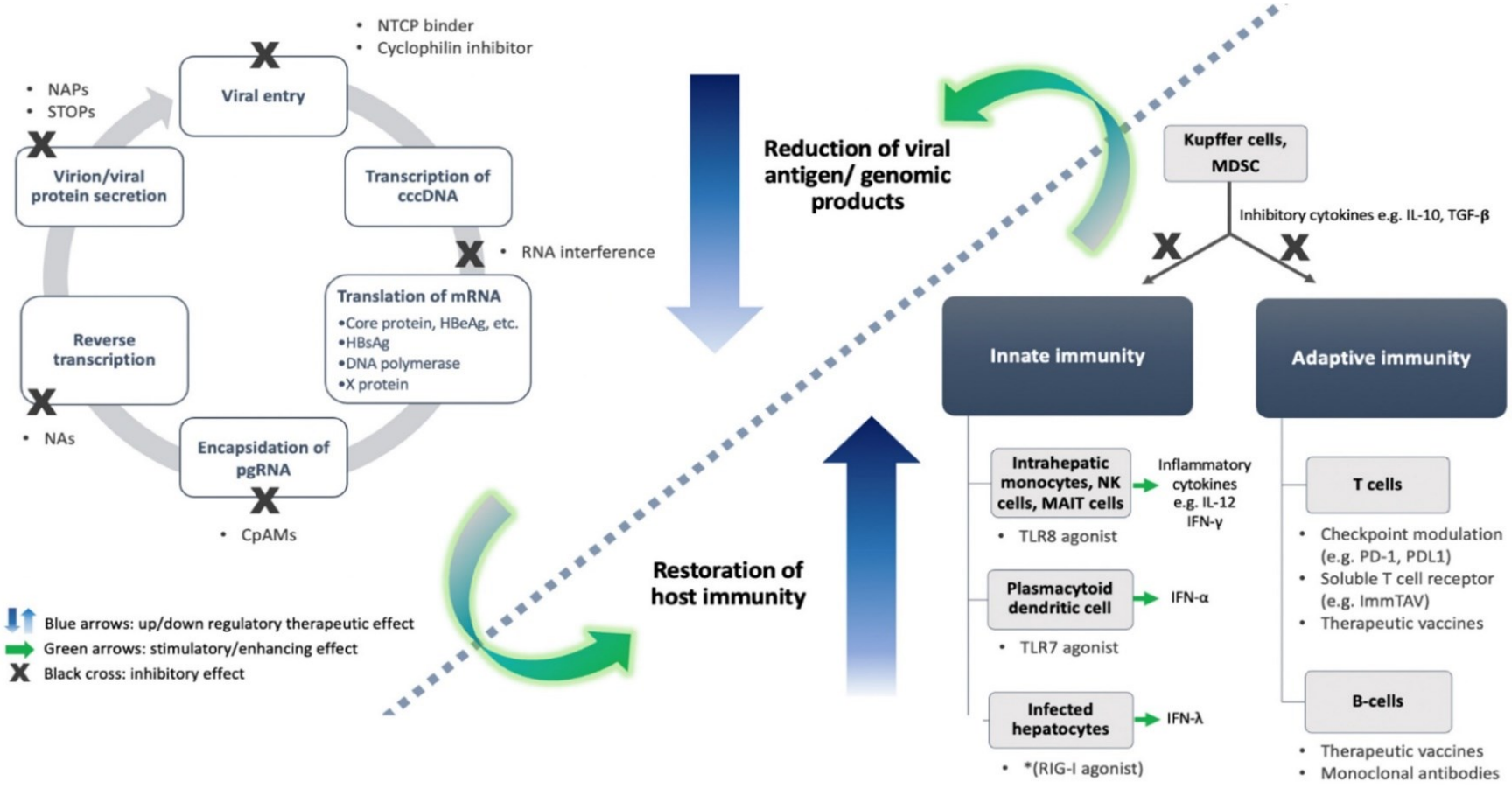
Background: PD-L1 and Chronic Hepatitis B (CHB)



- **Blockade of PD-1/PD-L1 pathway may be a cure of CHB.**

Chen, L., et al., Journal of immunology, 2007, 178(10): 6634-41.

Combination therapy might optimize the chance of a functional cure in CHB



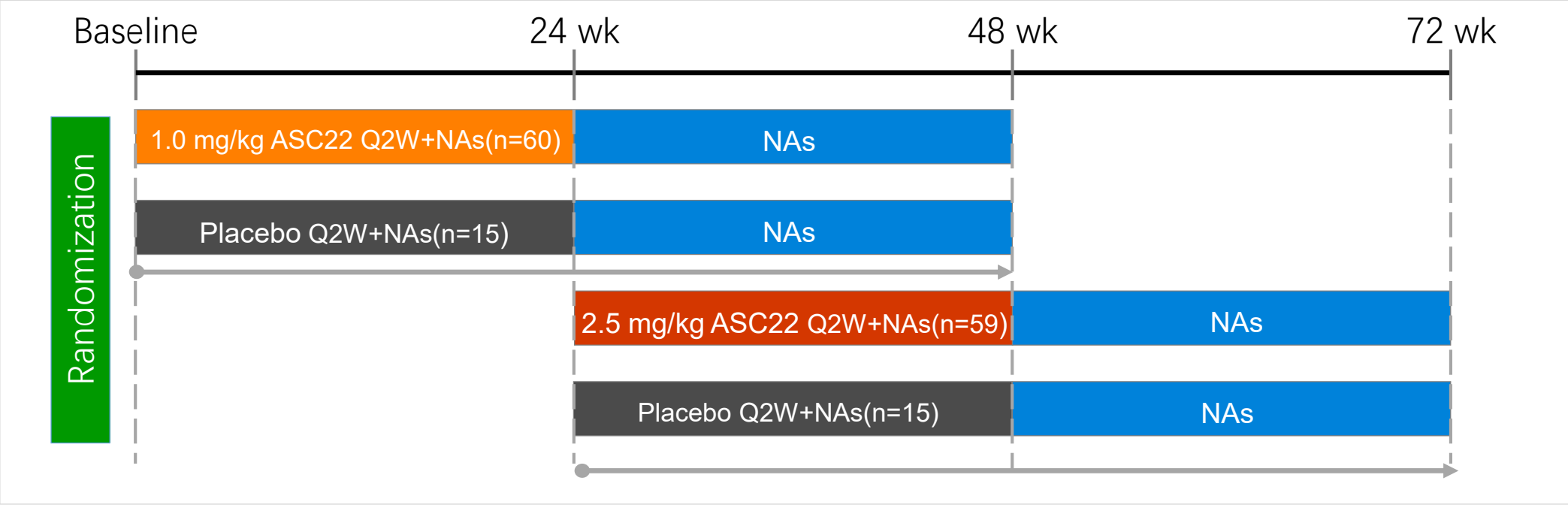
- **Combination therapy of nucleos(t)ide analogue, a novel virus-directing agent, and/or an immunomodulatory agent will be the likely approach to optimize the chance of a functional cure in CHB.**

Mak, L. Y., et al., Viruses, 2021, 13(6):

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, HBeAg negative.**
- **To assess efficacy and safety of ASC22 in CHB patients**

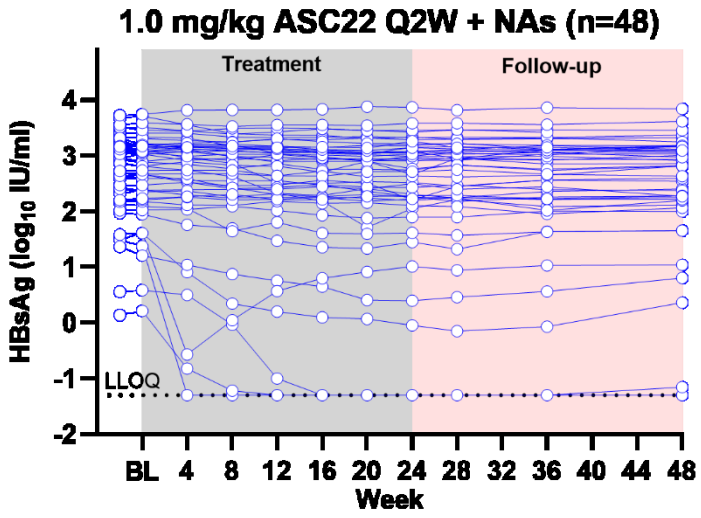


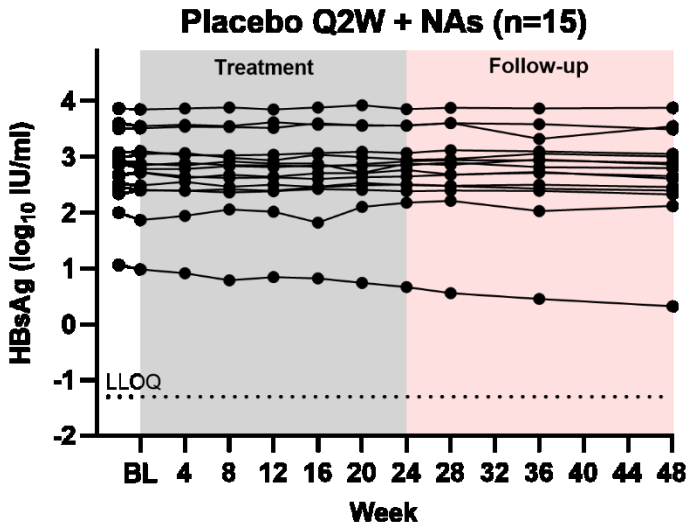
■ **Report of 1.0mg/kg ASC22 final result**

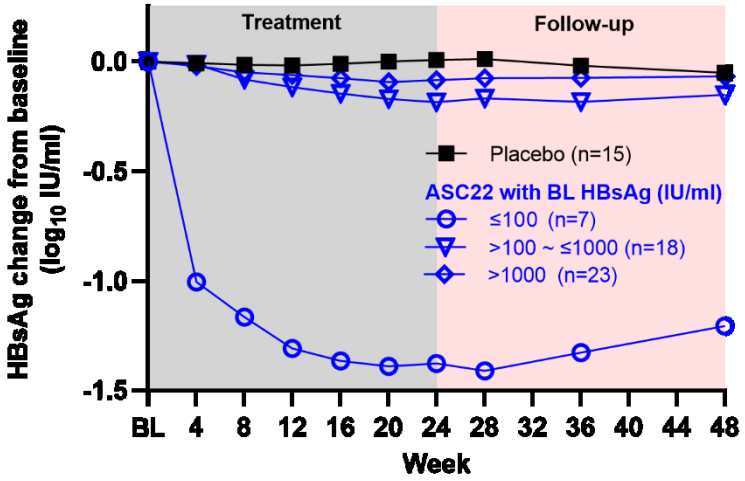
Demographic and Baseline Characteristics

	1.0 mg/kg ASC22 + NAs (n=60)	Placebo +NAs (n=15)
Median age, yrs (range)	40.5 (23 ~ 63)	40 (32 ~ 48)
Male, n (%)	41 (68.3%)	12 (80%)
Chinese,n(%)	60 (100%)	15 (100%)
Median BMI, kg/m^2 (range)	23 (18 ~ 29)	24 (20 ~ 28)
Median HBsAg, log_{10}IU/ml (range)	2.9 (-1.3 ~ 3.7)	2.8 (1.0 ~ 3.9)
HBsAg ≤ 100 IU/ml, n (%)	10 (17%)	2 (13%)
HBeAg negative, n (%)	60 (100%)	15 (100%)
Median ALT, U/l (range)	22.0 (10.0 ~ 65.0)	19.0 (8.0 ~ 55.0)
Median AST, U/l (range)	23.0 (11.0 ~ 64.0)	21.0 (11.0 ~ 31.0)
Peg-IFN treatment history, n (%)	22 (36.6)	11(73.3%)
Peg-IFN duration prior to study (years), Median (range)	1.0(0.2~4.2)	1.0(0.4~1.6)
NA treatment history, n (%)	60(100%)	15(100%)
NAs duration prior to study (years), Median (range)	5.2 (0.8~19.0)	4.4(0.5~13.0)

ASC22 plus NAs can induce HBsAg Reduction

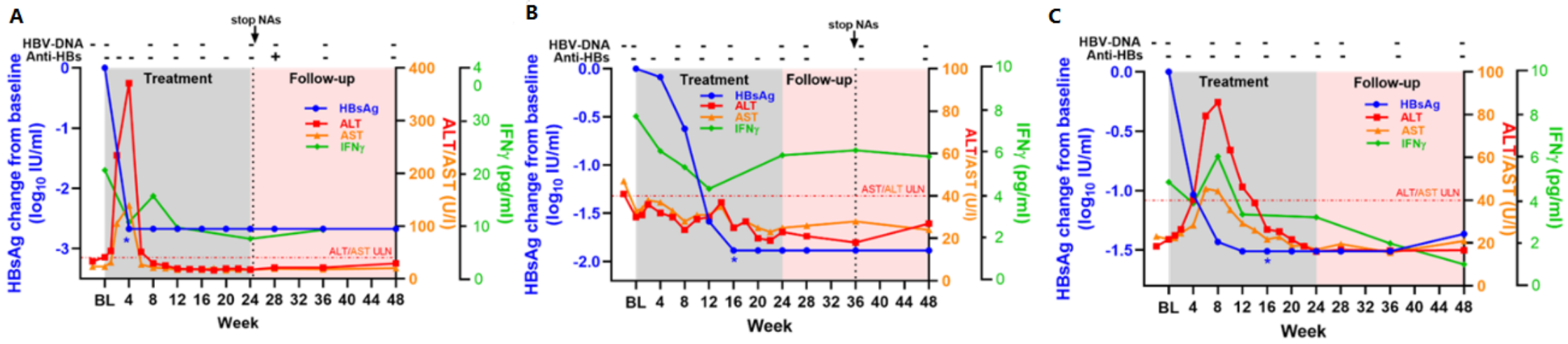






- Patients with baseline HBsAg ≤100 IU/ml had more significant HBsAg reduction.
- Three patients with baseline HBsAg ≤100 IU/ml (3/7, 42.9%) obtained sustained HBsAg loss (below LLOQ: 0.05 IU/ml).

Three patients obtained sustained HBsAg loss



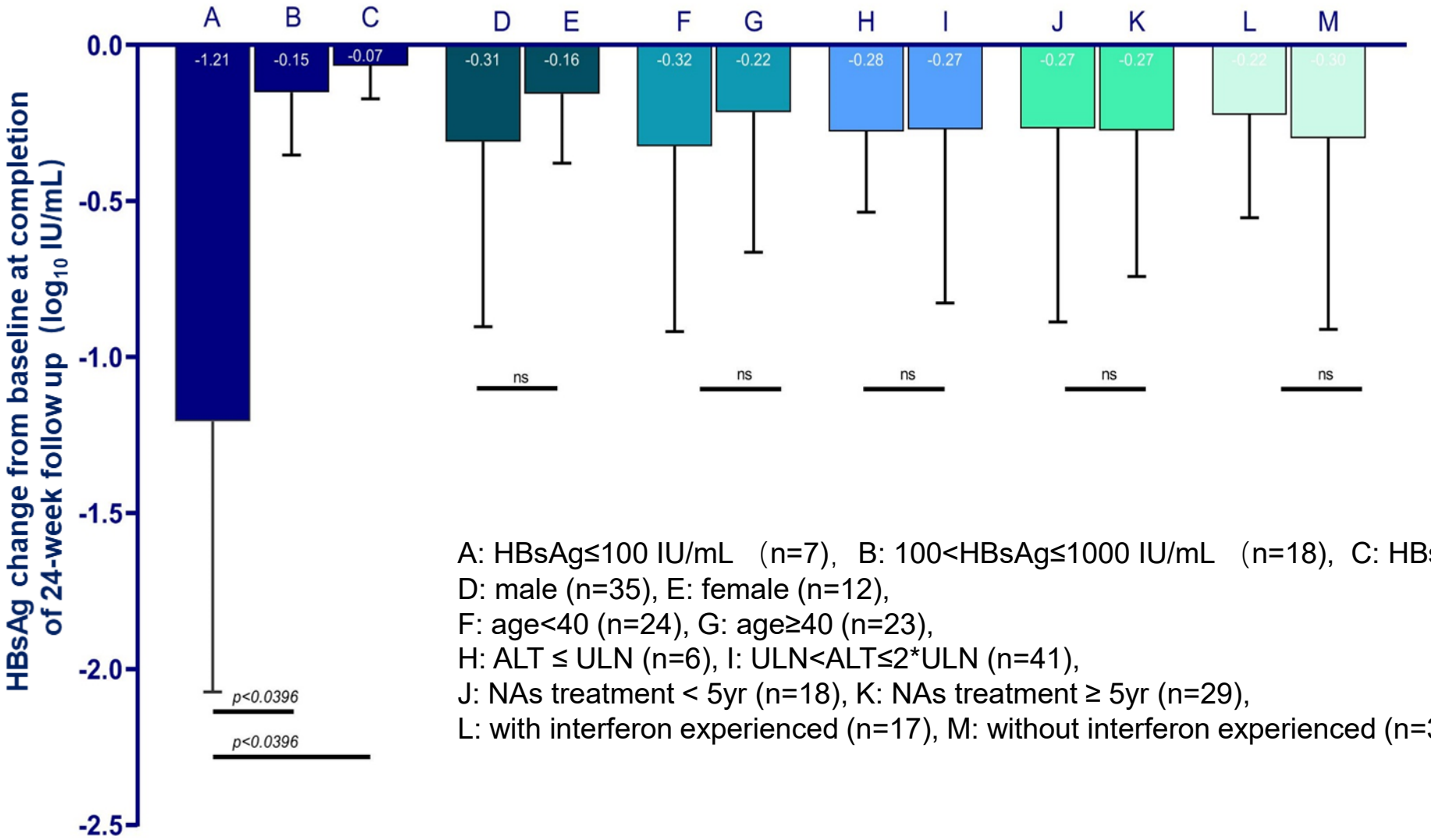
- HBsAg loss occurred in three patients treated with ASC22 at Weeks 4, 16 and 16, respectively, as shown in A, B and C
- Patients A and B stopped NA treatment 3 days and 3 months later after 24-week ASC22 treatment, and HBsAg remained negative until end of study.
- Patient C was still on NAs therapy after HBsAg loss, and had HBsAg level of 0.07 IU/ml at end of study. However, HBsAg became undetectable again at the recent visit 41 weeks later after study.

HBsAg reduction are correlated with pre-treatment HBsAg level

1.0 mg/kg ASC22 group, HBsAg change from the baseline (log_{10} IU/ml) (per-protocol population)

Group	n	Treatment				Follow-up			
		Week 12 LS-means (s.e.) 95% CI	P	Week 24 LS-means (s.e.) 95% CI	P	Week 12 LS-means (s.e.) 95% CI	P	Week 24 LS-means (s.e.) 95% CI	P
Baseline HBsAg (IU/ml)									
≤100	7	-1.308(0.115) -1.538 , -1.077		-1.377(0.126) -1.632 , -1.123		-1.328(0.130) -1.590 , -1.066		-1.206(0.133) -1.474 , -0.939	
101-1000	18	-0.117(0.071) -0.261 , 0.027	**<0.001**	-0.186(0.079) -0.345 , -0.027	**<0.001**	-0.184(0.081) -0.347 , -0.021	**<0.001**	-0.152(0.083) -0.319 , 0.015	**<0.001**
>1000	23	-0.062(0.063) -0.189 , 0.066		-0.085(0.070) -0.226 , 0.055		-0.075(0.072) * -0.220 , 0.069		-0.068(0.072) -0.210 , 0.074	

Other baseline characteristics have no impact on HBsAg changes



A: HBsAg≤100 IU/mL （n=7），B: 100<HBsAg≤1000 IU/mL （n=18），C: HBsAg>1000 IU/mL （n=23）
D: male (n=35), E: female (n=12),
F: age<40 (n=24), G: age≥40 (n=23),
H: ALT ≤ ULN (n=6), I: ULN<ALT≤2*ULN (n=41),
J: NAs treatment < 5yr (n=18), K: NAs treatment ≥ 5yr (n=29),
L: with interferon experienced (n=17), M: without interferon experienced (n=30)

Safety assessment of ASC22 in CHB patients

Patient, n(%)	ASC22 1.0 mg/kg + NAs (N=60)		Placebo + NAs (N=15)	
	Number of cases	Number of patients (%)	Number of cases	Number of patients (%)
Any AE	318	54 (90.0)	50	12 (80.0)
Any Grade 3-4 AE	7	4 (6.7)	2	2 (13.3)
Any Serious AE	3	3 (5.0)	0	0 (0.0)
Investigations	88	23 (38.3)	26	6 (40.0)
ALT increased	27	18 (30.0)	2	2 (13.3)
AST increased	24	14 (23.3)	0	0 (0.0)
Infections and infestations	34	25 (41.7)	7	5 (33.3)
Endocrine disorders	13	7 (11.7)	0	0 (0.0)
Metabolism and nutrition disorders	35	10 (16.7)	5	2 (13.3)
Skin and subcutaneous tissue disorders	36	25 (41.7)	0	0 (0.0)
Hepatobiliary disorders	5	5 (8.3)	1	1 (6.7)

- Most AEs were Grade 1-2, and with outcomes of resolved. ASC22 1.0 mg/kg was generally well tolerated in CHB patients.

Key Takeaways

- **ASC22 Q2W plus NAs can induce HBsAg decline, even sustained HBsAg loss, in CHB patients on NAs, especially in those with baseline HBsAg ≤100 IU/ml.**
- **Subcutaneous administration of ASC22 Q2W for 24 weeks is shown to be safe and well-tolerated.**
- **HBsAg reduction upon ASC22 treatment was correlated with pre-treatment HBsAg level.**

Thank you

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