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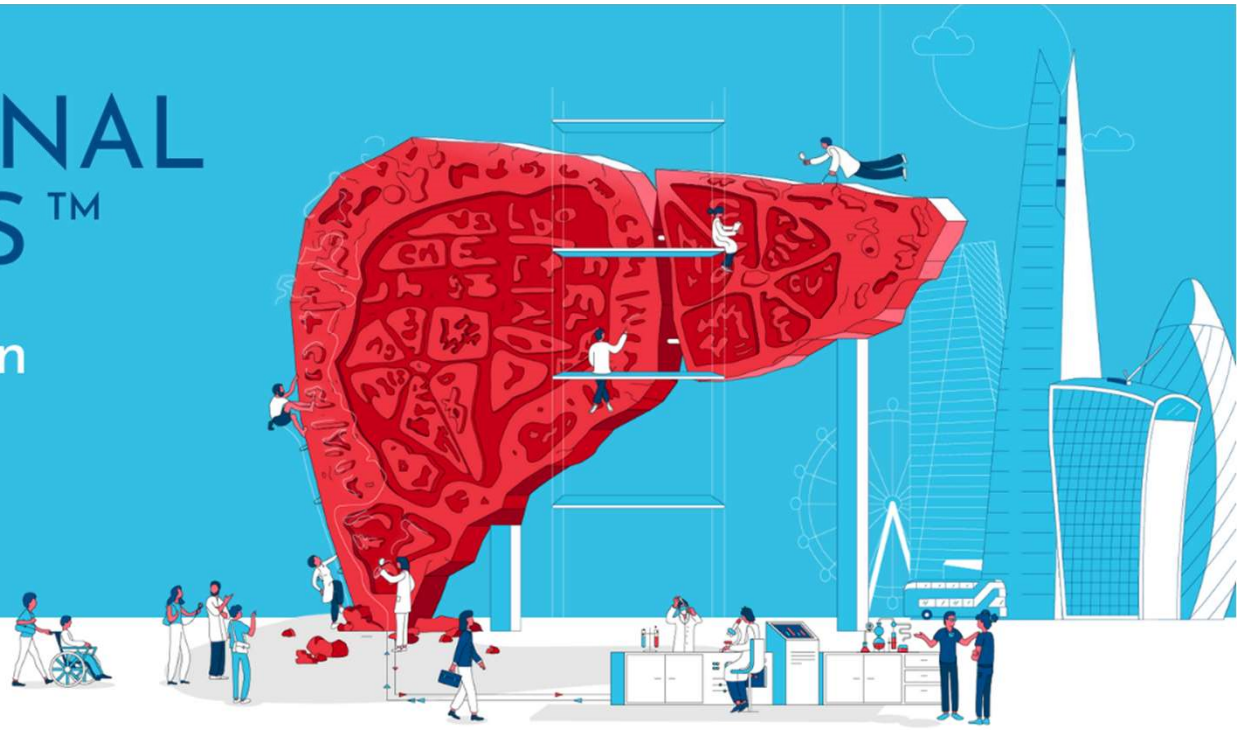

ALT flares were linked to HBsAg reduction, seroclearance and seroconversion: interim results from a Phase IIb study in chronic hepatitis B patients with 24-week treatment of subcutaneous PD-L1 antibody ASC22 (Envafolimab) plus nucleos(t)ide analogs

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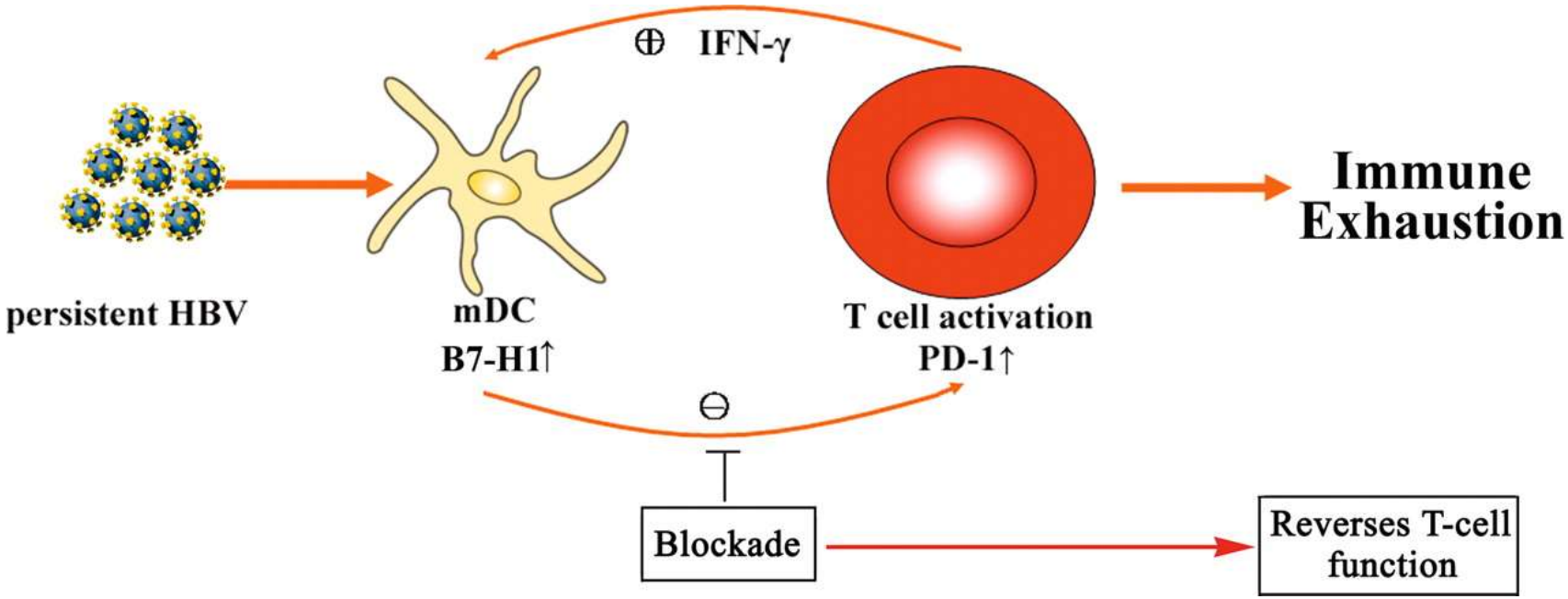
Background: PD-L1 and Chronic Hepatitis B (CHB)



- **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.

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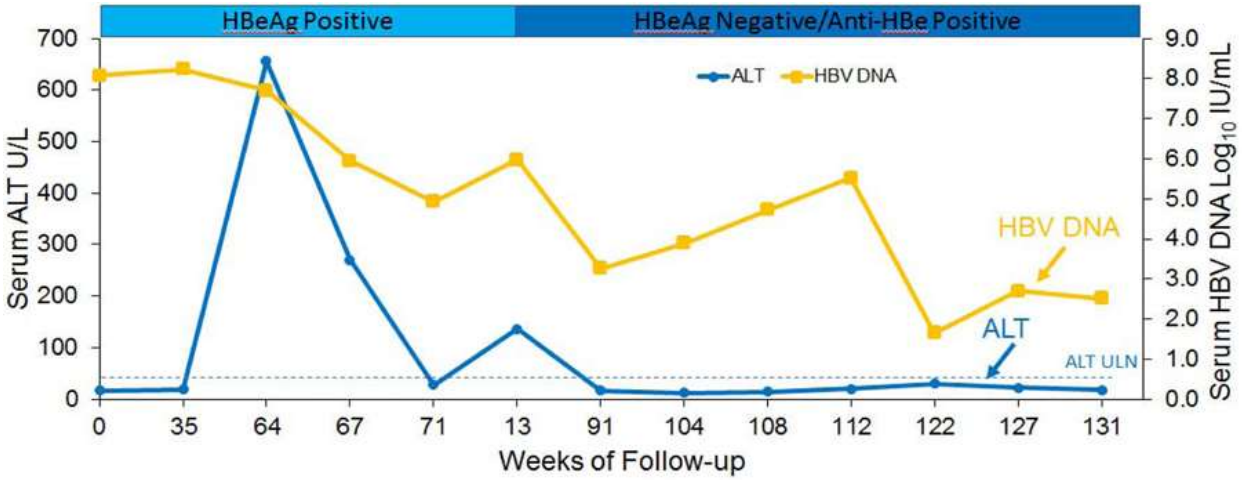
Background: Alanine Aminotransferase (ALT) Flares

Acute elevation in serum ALT level or flares occur from time to time during the natural course of chronic infection, thought to represent attempts at host immune-mediated viral clearance.



An ALT flare was defined as:

(1) an episode of ALT ≥5×ULN[1] (PEG-IFN-α alone or plus NAs) ; or

(2) a rise in ALT >2× ULN or >2x baseline ALT level[2] (NAs); or

(3) a rise in ALT ≥5× ULN or >3x baseline ALT level[3].

1. Ghany M et al. The lancet. Gastroenterology & hepatology vol. 5,4 (2020): 406-417.
2. Wong D et al. Liver Int. 2018;38(10):1760-1769.
3. Lok AS, Lai CL. J Hepatol 1990; 10(1): 29–34.

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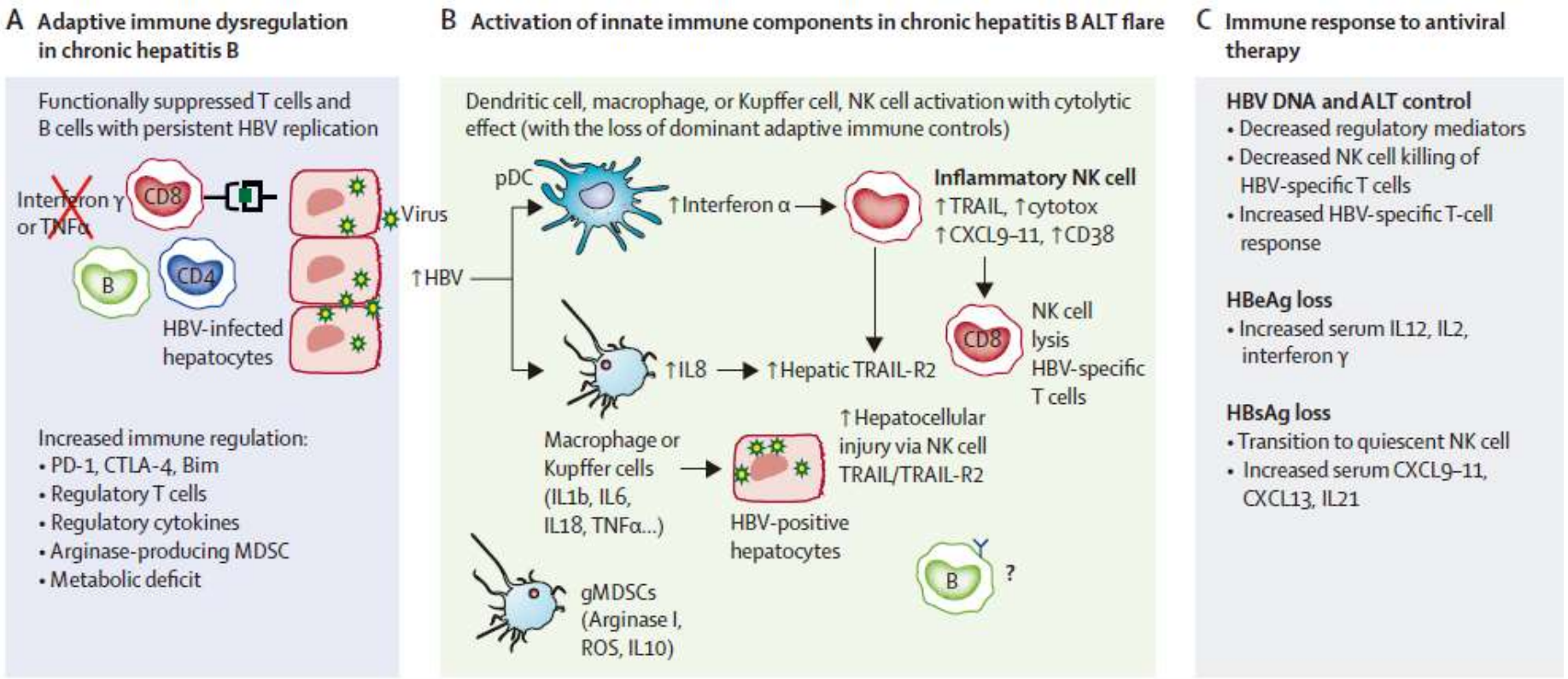
Background: Proposed Immune Components in CHB ALT Flare



Ghany M et al. The lancet. Gastroenterology & hepatology vol. 5,4 (2020): 406-417.

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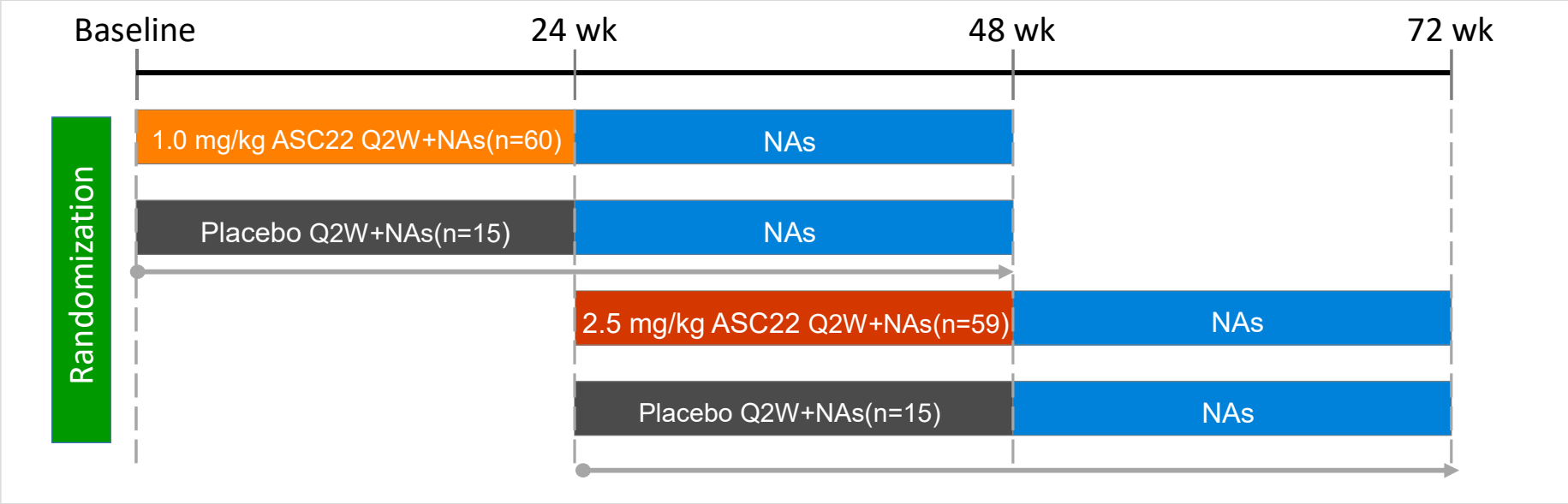
ASC22 Phase IIb Clinical Trial (NCT04465890)

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**



Interim Report of ASC22 Phase IIb Clinical Trial

Based on the 75 patients in 1.0 mg/kg ASC22 cohort:

ASC22 1.0 mg/kg + Nucleos(t)ide Analogs (NAs): n=60
Placebo (PBO) + NAs: n=15

- **Safety population: 60 + 15**
- **Full analysis population: 48 + 15**

(10 drop-outs from study; 1 without complete dosing; 1 with BL HBsAg <0.05 IU/ml)

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)

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

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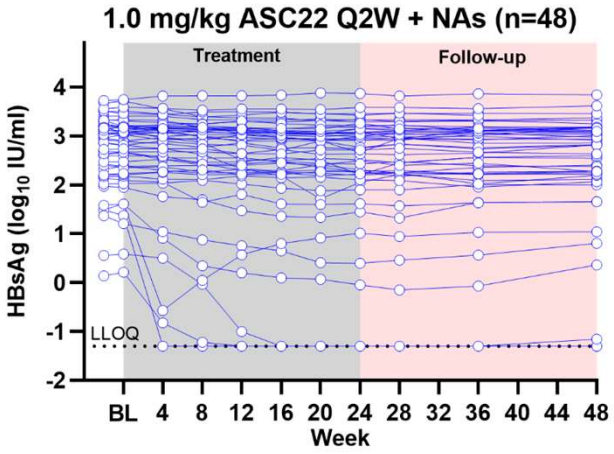
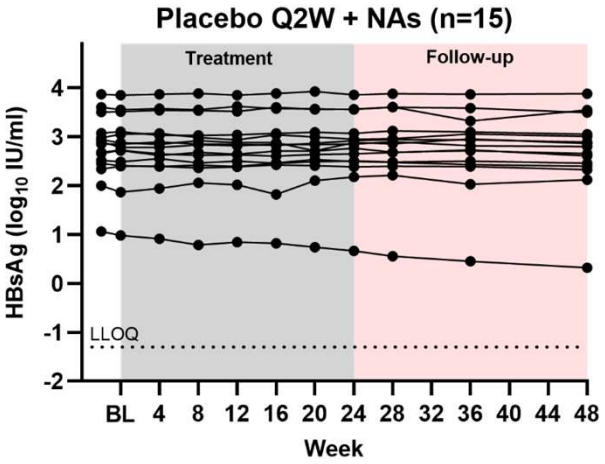
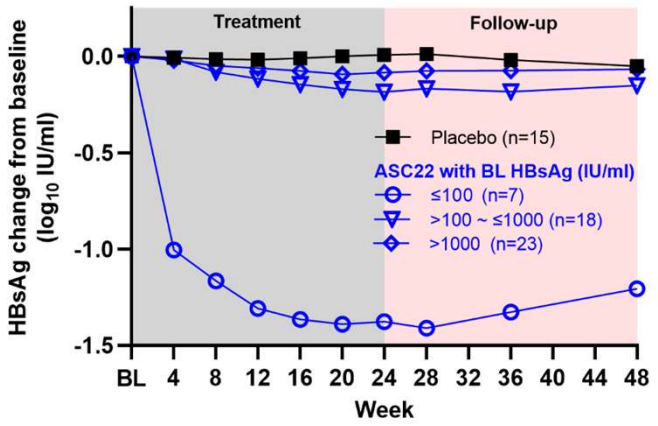
ASC22 plus NAs can induce HBsAg Reduction







- **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).**
- Circulating serum HBsAg level is a biomarker for HBV-specific T and B cell responses in patients with CHB[1].

1. Kim JH, et al. *Sci Rep*. 2020;10(1):1835.

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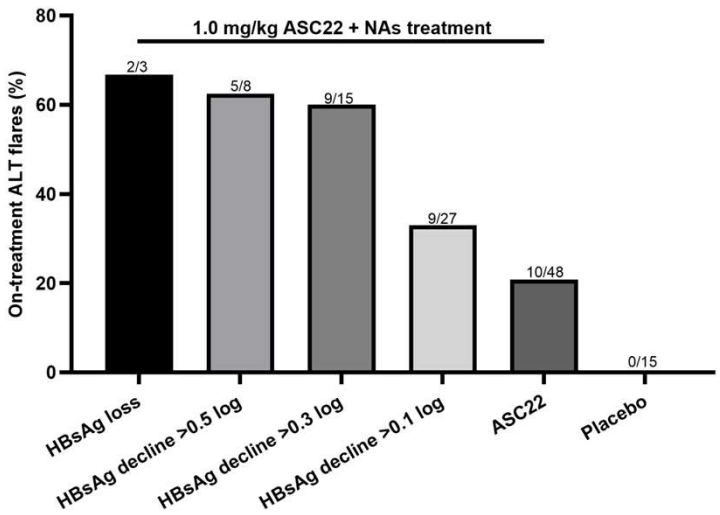
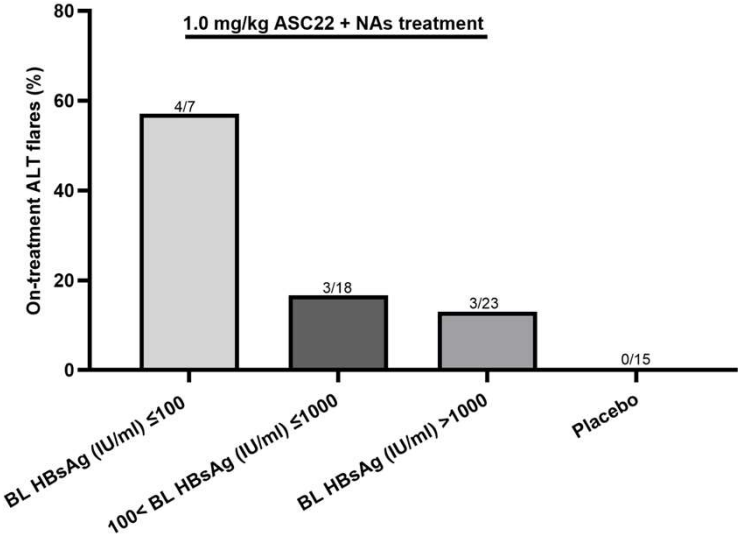
On-treatment ALT flares were observed only in ASC22 group

An ALT/AST flare is defined as ALT/AST greater than 3-fold baseline level and more than 2X ULN.





- ALT flares were observed in 10/48 (21%) patients in ASC22 group compared to none in PBO group.
- **ALT flares were more frequently occurred in patients with more HBsAg reduction or with lower baseline (BL) HBsAg.**

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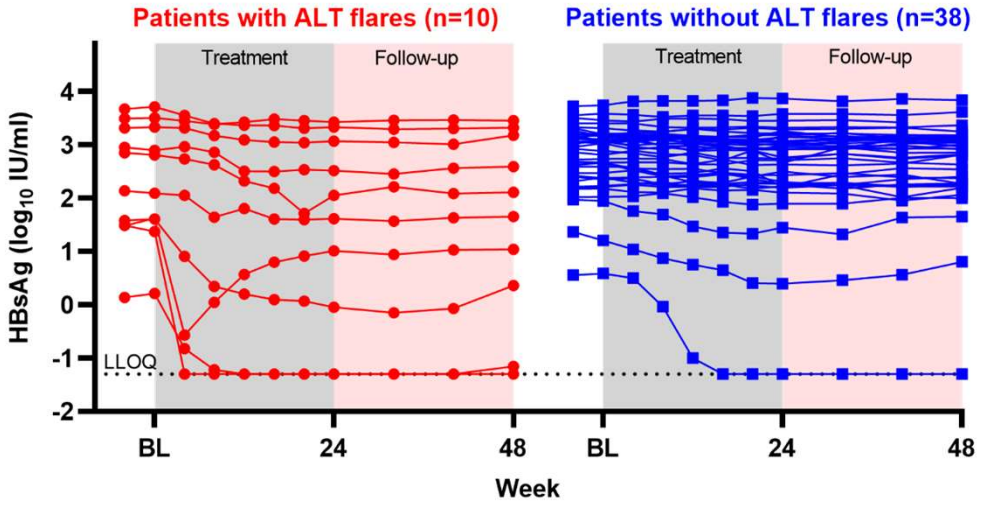
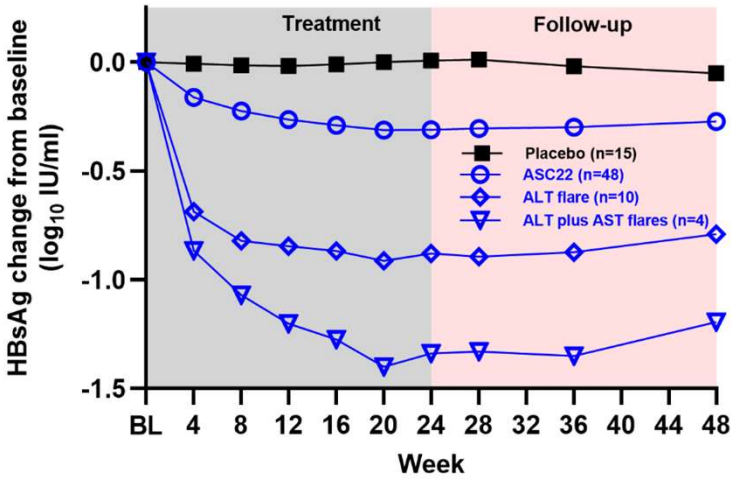
Patients with ALT flares had more significant HBsAg decline





- Nine out of 10 patients with ALT flares showed an obvious downward trend of serum HBsAg.
- **Patients with ALT/AST flares had more HBsAg reduction**.
- Two out of three patients with sustained HBsAg loss experienced ALT flares.

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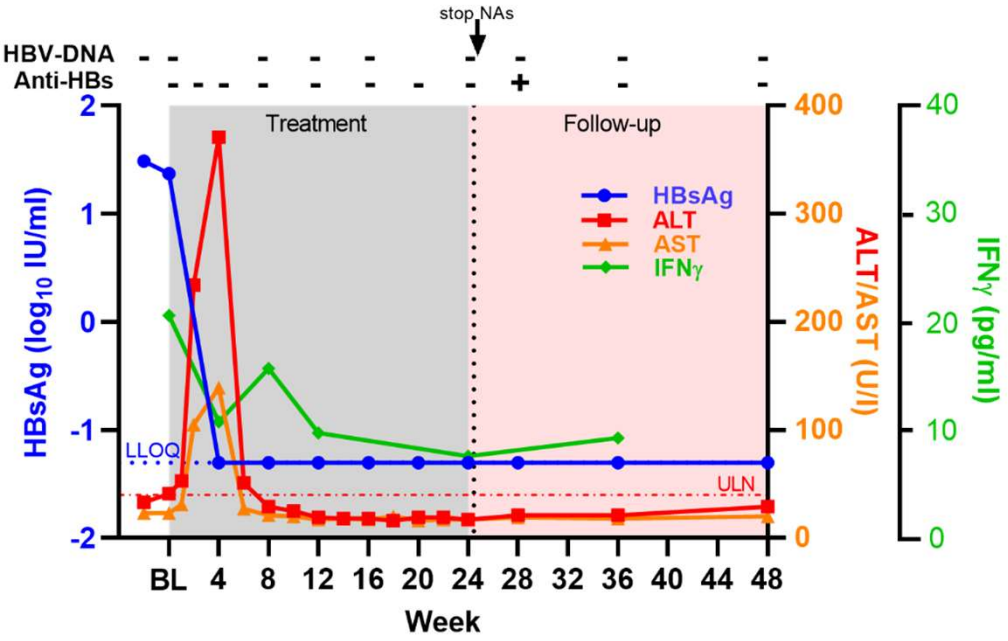
ALT flares and seroconversion of HBsAg to anti-HBs



- One patient obtained sustained HBsAg loss starting at Week 4 after 2 doses of ASC22 and experienced a transient seroconversion of anti-HBs at Week 28.
- This patient stopped NAs treatment 3 days after 24-week treatment of ASC22, and HBsAg still remained negative in the end of study.

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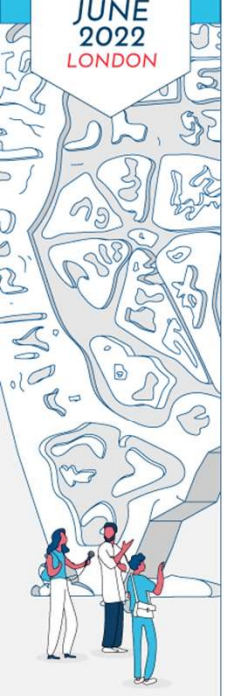

ALT flares might be used to monitor patient's response

HBsAg decline (log_{10} IU/ml), mean (s.d.)	n	Week 12	*P*	Week 24	*P*	Week 36	*P*	Week 48	*P*
Treatment arm									
ASC22	48	-0.264 (0.528)	**0.0027**	-0.311 (0.554)	**0.0005**	-0.299 (0.548)	**0.0029**	-0.271 (0.525)	**0.0185**
Placebo	15	-0.017 (0.074)		0.008 (0.130)		-0.020 (0.164)		-0.051 (0.188)	
ASC22 arm (n=48)									
Baseline HBsAg (IU/ml)									
≤100	7	-1.308 (0.762)		-1.377 (0.788)		-1.328 (0.849)		-1.206 (0.868)	
>100 ~ ≤1000	18	-0.117 (0.152)	**<0.0001**	-0.186 (0.235)	**0.0024**	-0.184 (0.204)	**0.0036**	-0.152 (0.200)	**0.0101**
>1000	23	-0.062 (0.108)		-0.085 (0.128)		-0.075 (0.118)		-0.071 (0.104)	
ALT flare									
Yes	10	-0.847 (0.816)	**0.0193**	-0.878 (0.815)	**0.0218**	-0.874 (0.822)	**0.0212**	-0.790 (0.790)	**0.0275**
No	38	-0.111 (0.275)		-0.162 (0.344)		-0.147 (0.323)		-0.130 (0.318)	
AST flare									
Yes	4	-1.202 (1.101)	0.1597	-1.339 (1.060)	0.1158	-1.350 (1.049)	0.1158	-1.194 (1.082)	0.1588
No	44	-0.179 (0.361)		-0.218 (0.388)		-0.203 (0.374)		-0.185 (0.360)	

- **ASC22 can induce serum HBsAg decline.**
- **HBsAg reduction is correlated with baseline HBsAg level and on-treatment ALT flares.**

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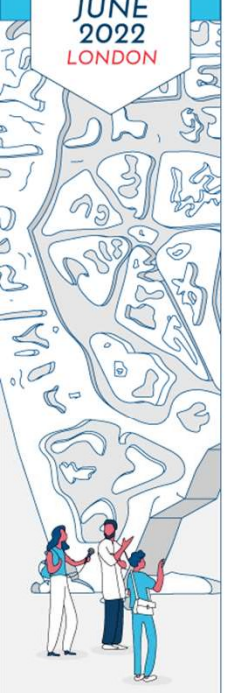

Safety assessment of ASC22 in CHB patients

Patient, n(%)	1.0 mg/kg ASC22 + NAs (N=60)		Placebo + NAs (N=15)	
	Number of cases	**Number of patients (%)**	**Number of cases**	**Number of patients (%)**
Any AE	323	54 (90.0)	50	12 (80.0)
Any Grade 3-4 AE	8	5 (8.3)	2	2 (13.3)
Any Serious AE	4	4 (6.7)	0	0 (0.0)
Study drug related AEs	193	41 (68.3)	26	6 (40.0)
Any Grade 3-4 AE	3	3 (5.0)	0	0 (0.0)
Any Serious AE	0	0 (0.0)	0	0 (0.0)
irAEs	108	31 (51.7)	0	0 (0.0)
ALT increased	25	16 (26.7)	0	0 (0.0)
AST increased	21	12 (20.0)	0	0 (0.0)
Skin related irAEs	25	19 (31.7)	0	0 (0.0)
Hyper/hypothyroidism	14	7(11.7)	0	0 (0.0)

- Most AEs (97.5%) were Grade 1-2, and no study drug-related SAE was reported.
- Most common AEs in patients with ALT flares were Grade 1-2 AST increased.

Summary of ASC22 Phase IIb Study (1.0 mg/kg cohort)

- **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.
- ALT flares were more frequently occurred in patients with more HBsAg reduction or lower baseline HBsAg. **Antiviral ALT flares might be used to monitor patient's response to the CHB treatment**.

Thank you

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

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