Monotherapy with the Capsid Assembly Modulator ALG-000184 Results in High Viral Suppression Rates in Untreated HBeAg-Positive Subjects with Chronic Hepatitis B Virus Infection

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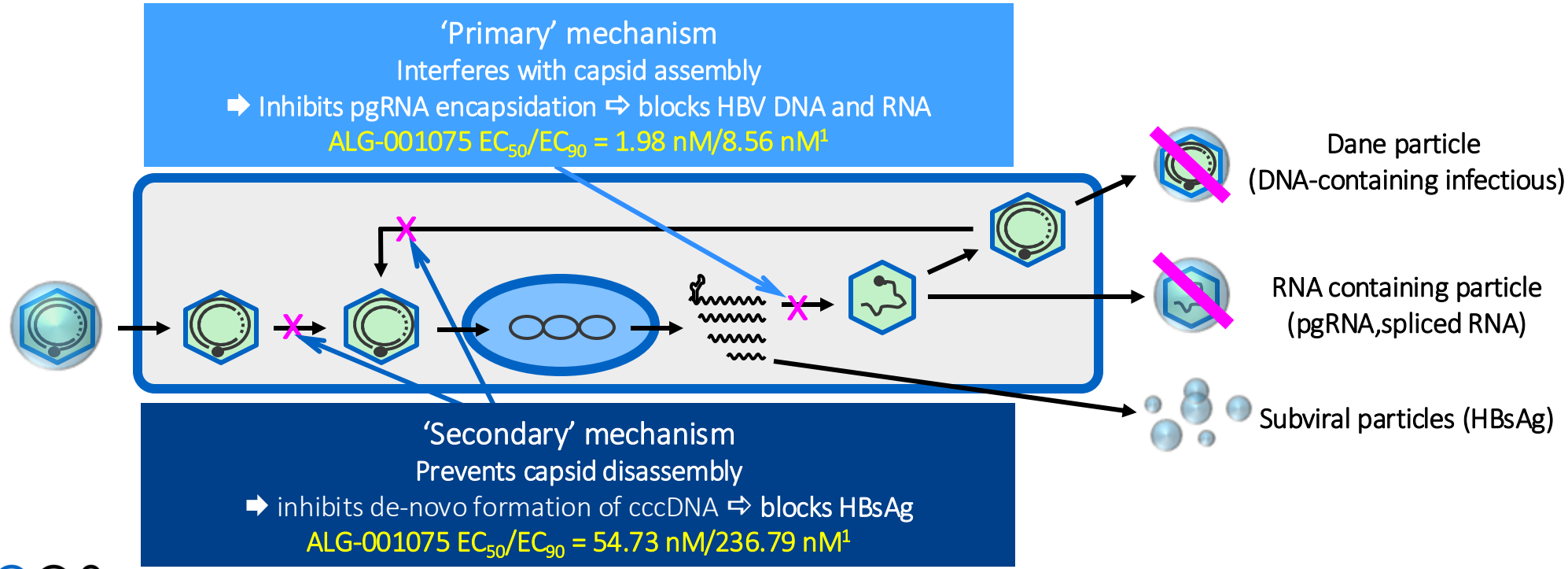
Disclosure of Conflict of Interest

- Member of Scientific Advisory Board for AbbVie, Abbott Diagnotics, Aligos Therapeutics, AiCuris, Antios Therapeutics, Arbutus Biopharma, Arrowhead Pharmaceuticals, Assembly Biosciences, Clear B Therapeutics, Dicerna Pharmaceuticals, Finch Therapeutics, Fujirebio Incorporation, GlaxoSmithKline, Gilead Sciences, Immunocore, Janssen, Precision BioSciences, Roche, Sysmex Corporation, Tune Therapeutics, Vir Biotechnology and Visirna Therapeutics.
- Speaker for Fujirebio Incorporation, Gilead Sciences, Roche, Sysmex Corporation
- Grant/research support from AbbVie, Assembly Biosciences, Arrowhead Pharmaceuticals, Fujirebio Incorporation, Gilead Sciences, Immunocore, Sysmex Corporation and Roche
- Data Safety Monitoring Board for Aligos Therapeutics, Suzhou Ribo Life Science Co.Grant/research support from AbbVie, Assembly Biosciences, Arrowhead Pharmaceuticals, Fujirebio Incorporation, Gilead Sciences, Immunocore, Sysmex Corporation and Roche

Background

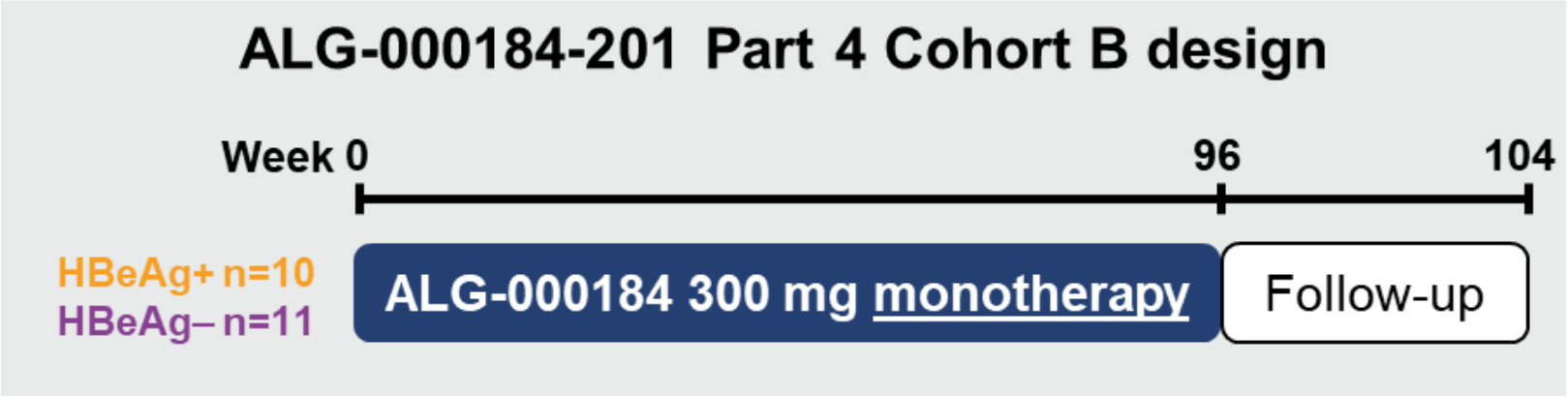
- Importance of **HBV DNA Suppression:** Achieving undetectable levels of HBV DNA using most sensitive assays crucial for effective viral control, reducing risk of liver disease progression. [WHO 2015, AASLD 2018, EASL 2017].
- **ALG-000184:** a prodrug of a novel CAM, ALG-001075, with potent in vitro anti-HBV activity through a dual mechanism-of-action (MOA):



1. Sandrine Vendeville et. al, Journal of Medicinal Chemistry 67:23

Background

- **ALG-000184-201 Study:** An ongoing Phase 1 study has shown favorable safety and potent antiviral activity in treatment naive or current not treated chronic HBV infection subjects receiving 300 mg ALG-000184 monotherapy ≤ 92 weeks [AASLD 2024 poster]:
  - **Significant Reductions:** Multiple log declines in HBV DNA, RNA and all HBV antigen levels were detected;
  - **No Breakthrough:** No virologic breakthrough was observed in any subjects.
- **Emerging Data:** Efficacy and safety data in HBeAg-positive subjects receiving 300 mg ALG-000184 monotherapy for ≤ 96 weeks.



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Baseline Characteristics in TN/CNT HBeAg+ Subjects 300 mg ALG-000184 monotherapy for ≤ 96 weeks

Baseline Characteristics	TN/CNT HBeAg+ subjects N=10
Age, years, mean (SD)	36.8 (2.9)
Male, N (%)	7 (70)
Asian, N (%)	**9 (90)**
BMI, kg/m^2, mean (SD)	22.4 (0.8)
HBV Genotype B/C, N (%)	B: 5 (50); C: 4 (40); D: 1 (10)
HBV DNA, log_{10} IU/mL, mean (SD)	**8.0 (0.2)**
HBV RNA, log_{10} copies/mL, mean (SD)	**5.3 (0.4)**
HBsAg, log_{10} IU/mL, mean (SD)	**4.3 (0.1)**
HBeAg, log_{10} PEI U/mL, mean (SD)	**2.6 (0.3)**
HBcrAg, log_{10} U/mL, mean (SD)	**8.3 (0.2)**
ALT, U/L, mean (SD)	60.7 (36.9)

Treatment Naïve (TN) subjects are defined as participants who have never received treatment with HBV antiviral medicines (NA, interferon [IFN]), or investigational anti-HBV agents including a CAM;
Current-not-treated (CNT) subjects are defined as participants who have not been on treatment with approved (NA, IFN) or investigational HBV antiviral medicineswithin 6 months prior to randomization

All 10 subjects received at least 76 weeks of monotherapy
Majority were Asians (9/10)
High levels of HBV markers prior to dosing with ALG-000184

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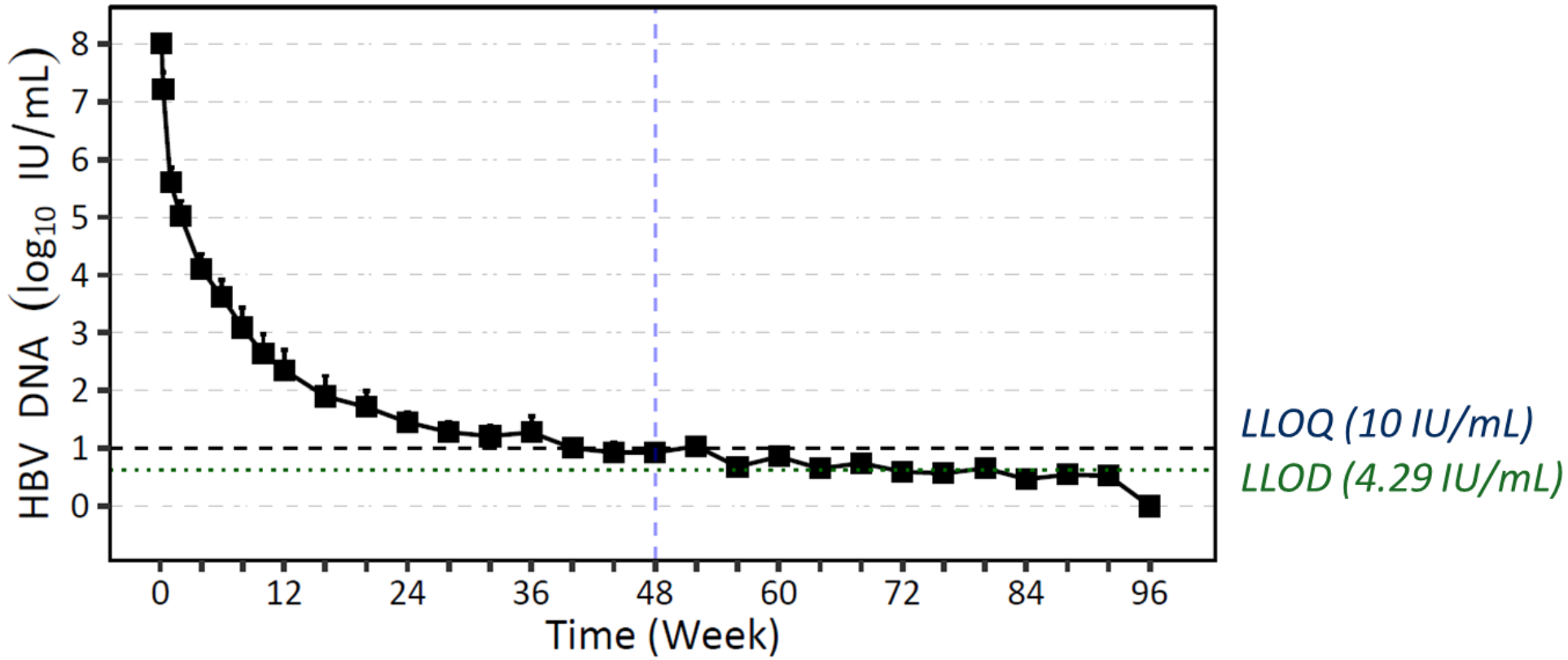
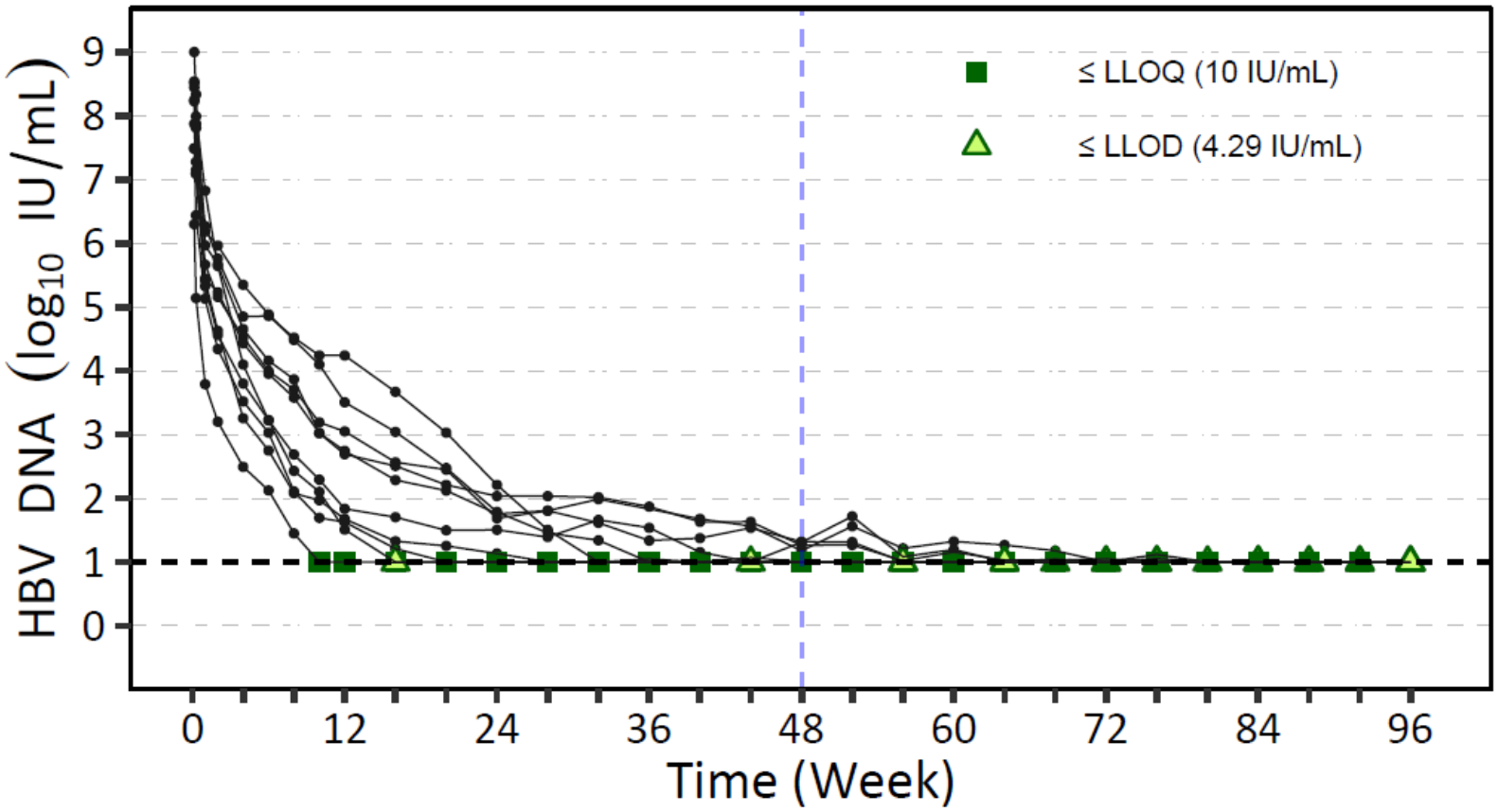
Mean HBV DNA Level
300 mg ALG-000184 monotherapy for ≤ 96 weeks



Number of subjects	10	10	10	10	10	10	10	9	3
Mean change from baseline	0	-5.7	-6.6	-6.7	-7.1	-7.2	-7.4	-7.7	-8.3
Median change from baseline	0	-5.8	-6.7	-7	-7.2	-7.2	-7.6	-7.8	-8.2
SEM	0	0.29	0.18	0.29	0.2	0.22	0.23	0.2	0.091

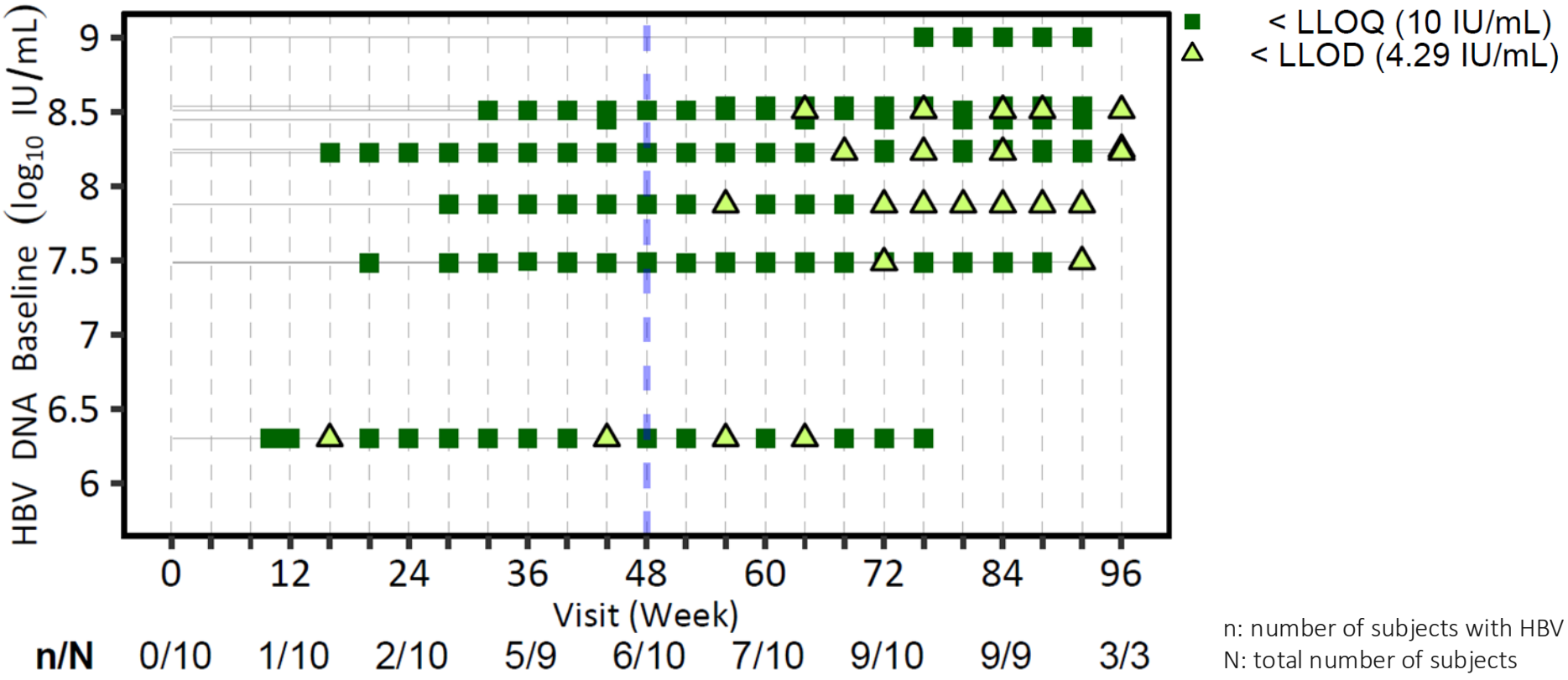
<LLOQ (target detected) imputed to 5 IU/mL; <LLOQ (target not detected) imputed to 1 IU/mL

Individual HBV DNA Levels
300 mg ALG-000184 monotherapy for ≤ 96 weeks



Number of subjects	10	10	10	9	10	10	10	9	3
n ≤ LLOQ (10 IU/mL)	0	1	2	5	6	7	9	9	3
n ≤ LLOD (4.29 IU/mL)	0	0	0	0	0	0	2	3	3

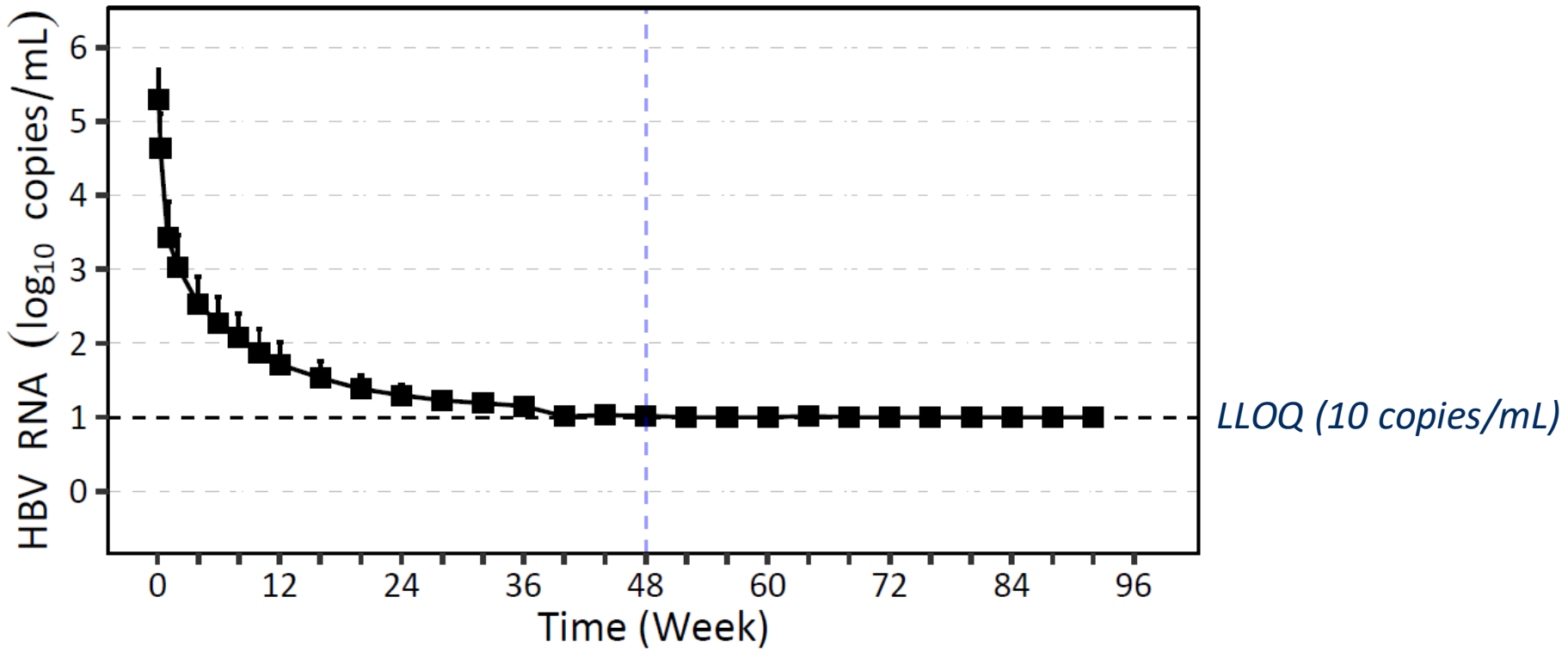
Individual Time to Reach HBV DNA < LLOQ or < LLOD
300 mg ALG-000184 monotherapy for ≤ 96 weeks



n: number of subjects with HBV DNA ≤ LLOQ
N: total number of subjects

Time to HBV DNA LLOQ or LLOD is dependent on baseline HBV DNA level
60% and 100% subjects achieved HBV DNA < LLOQ (10 IU/mL) at Week 48 and 96, respectively.
All 3 subjects who completed 96 weeks of monotherapy achieved DNA < LLOD (≤ 4.29 IU/mL)
No subject with 300 mg ALG-000184 monotherapy experienced virologic breakthrough

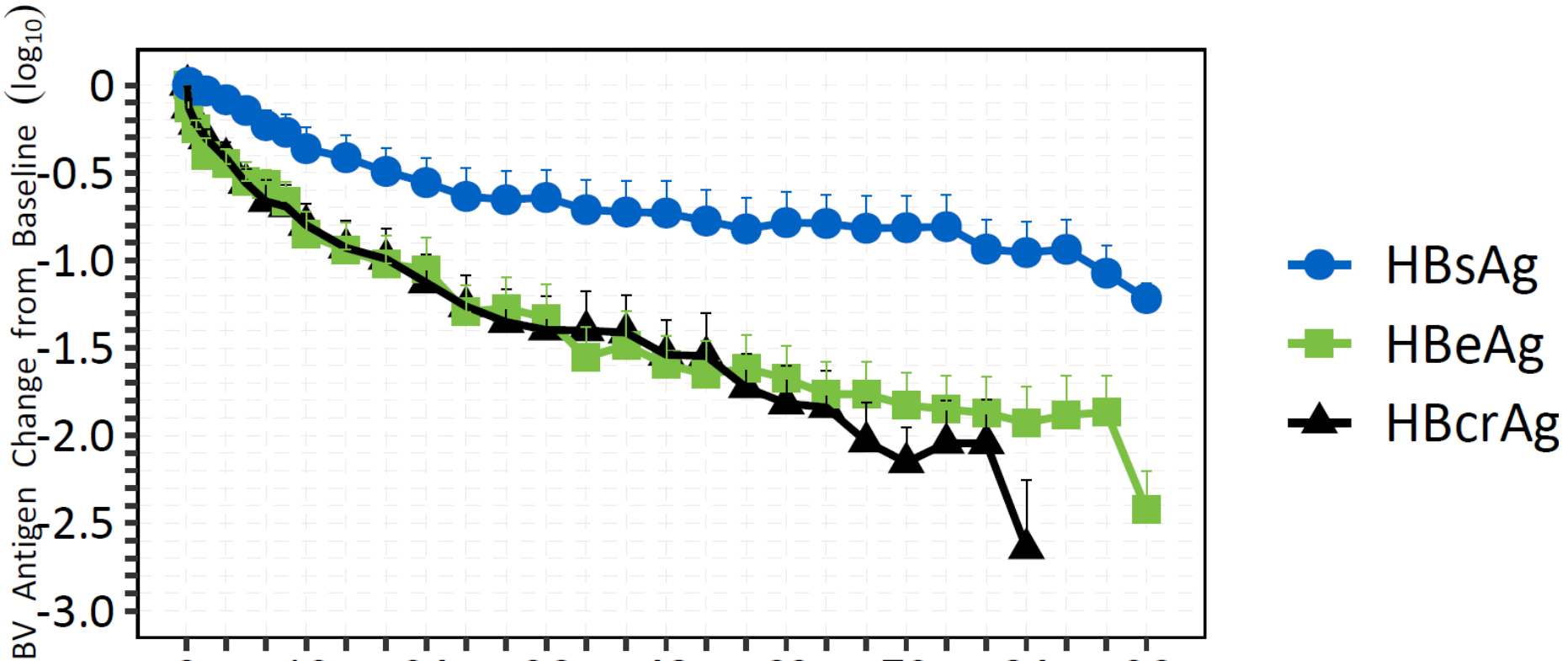
Mean HBV RNA Level
300 mg ALG-000184 monotherapy for ≤ 96 weeks



n/N	0/10	6/10	5/10	8/10	9/10	10/10	10/10	9/9
Mean change from baseline	0	-3.6	-4	-4.1	-4.3	-4.3	-4.3	-4.4
Median change from baseline	0	-3.3	-4.1	-4.4	-4.7	-4.8	-4.8	-5.1
SEM	0	0.3	0.38	0.4	0.42	0.42	0.42	0.46

n: number of subjects with HBV RNA ≤ LLOQ
N: total number of subjects

Mean Antigen Reductions
300 mg ALG-000184 monotherapy for ≤ 96 weeks



HBsAg	10	10	10	10	10	10	10	9	3
HBeAg	10	10	10	10	10	10	10	9	3
HBcrAg	10	10	10	10	10	10	9	3	

Units for HBsAg, HBeAg and HBcrAg are log_{10}IU/mL, log_{10}PEI U/mL and log_{10}U/mL, respectively

Safety
300 mg ALG-000184 monotherapy for ≤ 96 weeks

	TN/CNT HBeAg-positive subjects
Numbers of subjects with	N=10
at least one TEAE, n(%)	9 (90)
SAE	0
TEAE leading to study drug discontinuation	0
TEAE Grade ≥3	3 (ALT/AST elevations)

300 mg ALG-000184 monotherapy for up to 96 weeks has favorable safety profile. 3 Grade ≥3 TEAEs of ALT elevations with or without AST increase with preserved synthetic and excretory functions were not considered clinically concerning by ALT Flare Committee.
All resolved in setting of continued ALG-000184 dosing.

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Summary

300 mg ALG-000184 monotherapy in TN/CNT HBeAg-positive subjects for ≤ 96 weeks demonstrated:

- A favorable safety profile
- Persistent antiviral effect:
  - At Weeks 48 and 96, HBV DNA levels declined 7.1 and 7.7 log10 IU/mL, respectively; and 60% and 100% of subjects achieved sustained HBV DNA level < 10 IU/mL, respectively.
  - All subjects achieved HBV RNA < 10 IU/mL by Week 52 and maintained this level for the remaining treatment duration for up to 96 weeks.
  - All HBV antigens continued downward trends after the initial multiple log declines.
- No viral breakthrough was observed in any subject.

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Conclusions

- These data suggest the substantial antiviral effect continued in the extended duration of 300 mg ALG-000184 monotherapy for up to 96 weeks.
- 300 mg ALG-000184 monotherapy is being developed as the backbone of a chronic suppression regimen for treatment of chronic HBV infection.

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Acknowledgement

Sincere gratitude to all individuals and organizations that contributed to this HBV data presentation.

- Heartfelt thanks go to the study participants for their willingness to engage in this important research;
- Appreciations for the dedication of the clinical site staff who facilitated the study.
- Gratitude to CRO Novotech for their invaluable insights and support.

These contributions have been essential to the success of this research.

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