Oral Once-Daily 300 mg ALG-000184, a Novel Capsid Assembly Modulator, Demonstrated Profound and Sustained Suppression of HBV DNA to < 10 IU/mL in All Treatment-Naïve (TN) or Currently-Not-Treated (CNT) Subjects with Chronic HBV Infection

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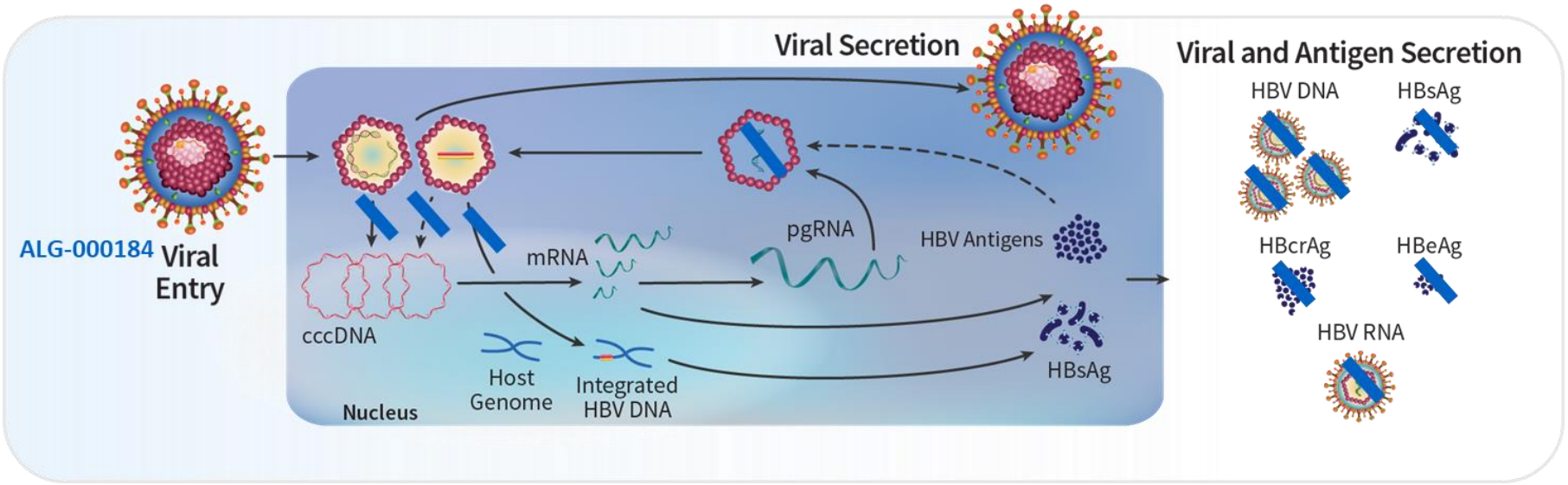
AASLD The Liver Meeting® NOV. 7–11, 2025

Disclosures

- Member of Scientific Advisory Board for AbbVie, Abbott Diagnostics, 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, and 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

Pevifoscorvir Sodium (ALG-000184), a Prodrug of CAM-E ALG-001075, Demonstrated Potent Dual Mechanism of Action to Suppress the Entire HBV Lifecycle in Vitro



1st MOA causes the formation of empty capsids
- —Reduces viral secretion (HBV DNA/RNA)
- —In vitro EC_{50} of ALG-001075: 0.53 – 0.64 nM[1]

2nd MOA prevents capsid disassembly at higher concentration of ALG-001075
- —Prevents establishment/replenishment of cccDNA[2],which produces HBcrAg/HBeAg/HBsAg
- —EC_{90} of ALG-001075 in vitro on HBsAg inhibition was 266 nM[3]

[1]Sandrine Vendeville et. al, The Discovery and Preclinical Profile of ALG-000184, a Prodrug of the Potent Hepatitis B Virus Capsid Assembly Modulator ALG-001075; Journal of Medicinal Chemistry Vol. 67:23 21126-21142; [2] Jordi Verheyen et. al, AASLD Poser #1251; [3] Pevifoscorvir sodium data was generated by Aligos on the parent compound ALG-001075. Studies conducted in vitro.

Pevifoscorvir sodium demonstrated a ~2-300-fold improvement in vitro potency (HBV DNA inhibition) compared to other known CAM-Es.

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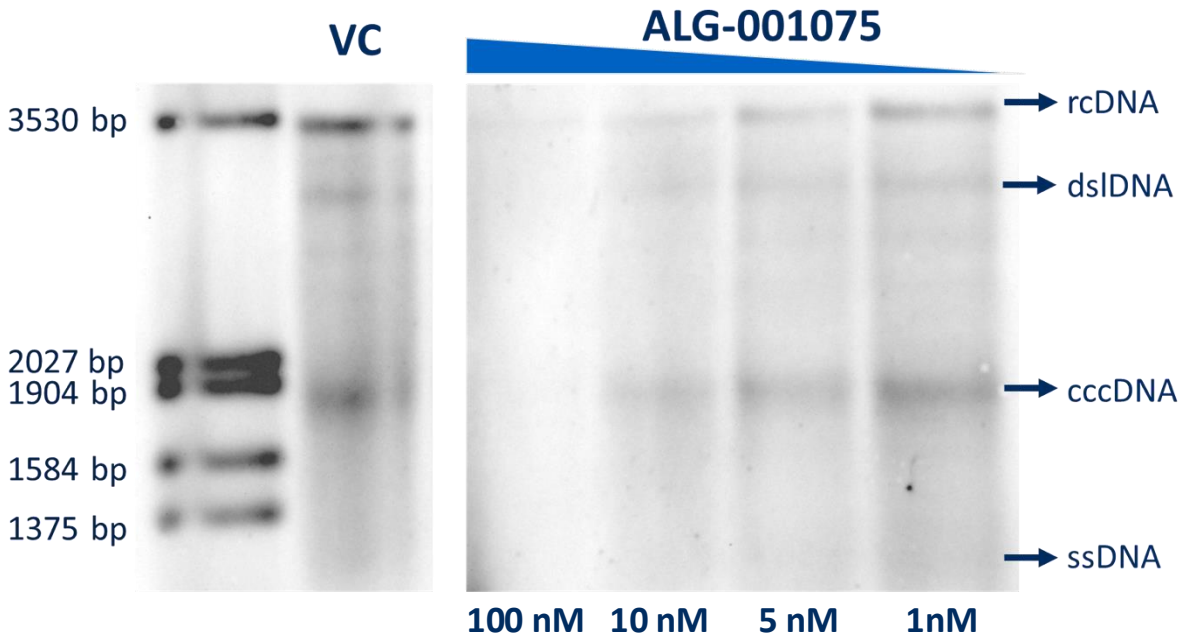
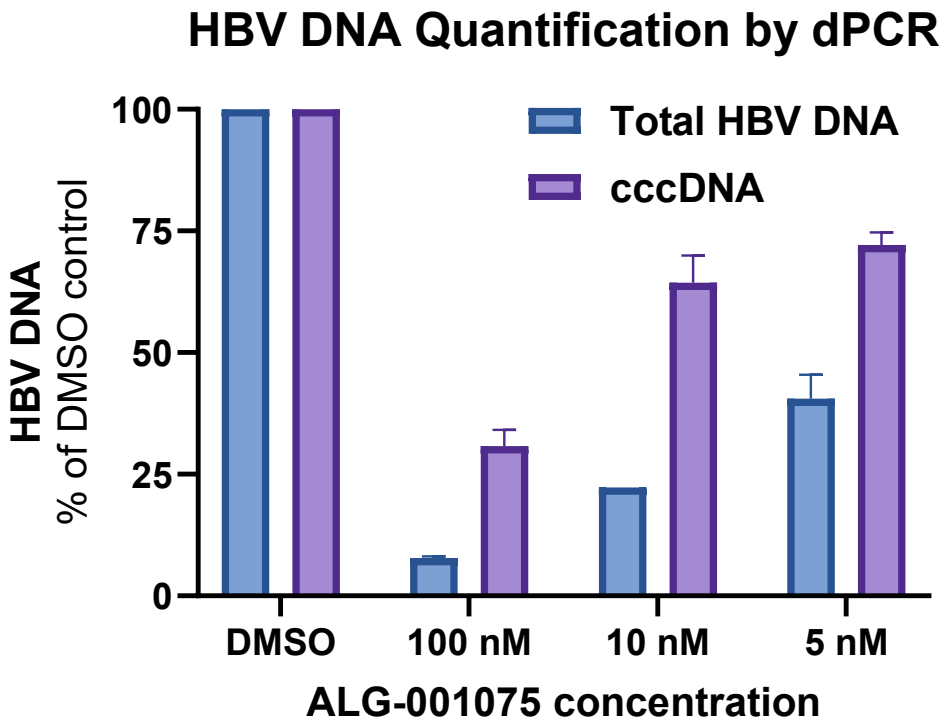
Pevifoscorvir Sodium

Prevention of HBV cccDNA Formation In Vitro





- **HBV-infected HepG2-NTCP cells**
- **ALG-001075 reduces rcDNA, dslDNA and cccDNA**

Jordi Verheyen et. al, AASLD 2025 Poser #1251.

ALG-001075 blocks cccDNA establishment in vitro

Study ALG-000184-201, a Multi-Part Phase 1 Study of Pevifoscorvir Sodium
Has Completed Evaluation in Healthy Volunteers and Subjects with Untreated Chronic HBV Infection

Parts 1 to 3 highlights[1,2]: (SAD/MAD and once daily 10-300 mg pevifoscorvir sodium oral doses x 28 days in TN/CTN subjects, NCT04536337)

- **PK:** Dose proportional increase in exposure with low to moderate variability
- **Safety:** All doses were well tolerated without any dose adjustment or early discontinuation
- **Efficacy**:
  - Rapid and profound reduction in HBV DNA and HBV RNA with the lowest dose (10 mg) achieving maximum HBV DNA reductions
  - Dose-related reduction in HBsAg noted at 100 mg and 300 mg pevifoscorvir sodium
    - Indicating engagement of CAM's secondary MOA
    - The only CAM to date that has demonstrated meaningful HBsAg reduction within 28 days
  - Comparable safety and efficacy between Asians (HBV genotype B, C) and non-Asians (HBV genotype A, D)

SAD-single dose escalation; MAD-multiple dose escalation; TN-treatment naïve; CTN-currently not treated; PK-pharmacokinetics.

1.Gane E, *et al.* Antiviral Therapy 2025 (in press) 2. Yuen MF, *et al.* Lancet Gastroenterology Hepatol 2025 (in press).

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Study ALG-000184-201
Long-Term Dosing in TN/CNT Subjects with Chronic HBV Infection
Part 4 Cohort Designs

China

Randomize
4 active:1 placebo

Cohort 2
HBeAg$^+$
N = 15

- Pevifoscorvir sodium 300 mg + ETV x ≤96 weeks → Follow-up (ETV only) x 8 weeks
- Placebo + ETV x 12 weeks → Pevifoscorvir sodium 300 mg + ETV x ≤96 weeks → Follow-up (ETV only) x 8 weeks

ROW

Cohort B
N=21
HBeAg$^+$ n=10
HBeAg$^-$ n=11

Pevifoscorvir sodium 300 mg monotherapy x ≤96 weeks (open label) → Follow-up (NA) x 8 weeks

HBeAg$^+$: HBeAg-positive; HBeAg$^-$: HBeAg-negative; ROW – rest of world; ETV – Entecavir; NA – nucleos(t)ide. NCT04536337.

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Study ALG-000184-201

Part 4 Baseline Characteristics

	HBeAg +			HBeAg -
	Part 4 Cohort 2		Part 4 Cohort B	Part 4 Cohort B
	ETV ×12 Weeks followed by 300 mg PEVY +ETV	300 mg PEVY +ETV	300 mg PEVY Monotherapy	300 mg PEVY Monotherapy
N	3	12	10	11
Age, years, mean (SD)	28 (4.6)	32.3 (10.2)	34.8 (9.1)	48.5 (10.2)
Female, N (%)	1 (33.3)	6 (50)	3 (30.0)	5 (45.5)
Asian, N (%)	3 (100)	12 (100)	9 (90.0)	3 (27.3)
BMI, kg/m^2, mean (SD)	22.3 (2.8)	22.2 (3.1)	22.4 (2.4)	26.0 (3.5)
HBV Genotype, N (%)	B: 1 (33) C: 2 (67)	B: 4 (33) C: 8 (67)	B: 5 (50), C: 4(40), D: 1 (10)	B:2(18), C:1(9), D:7(64), A:1(9)
HBV DNA, $\log_{10}$ IU/mL, mean (SD)	7.8 (1.1)	8.1 (0.8)	8.0 (0.8)	4.3 (0.7)
HBV RNA, $\log_{10}$ copies/mL, mean (SD)	6.5 (0.9)	6.7 (1.1)	5.3 (1.3)	2.0 (1.0)
HBsAg, $\log_{10}$ IU/mL, mean (SD)	4.1 (0.4)	4.5 (0.7)	4.3 (0.5)	3.5 (0.5)
HBeAg, $\log_{10}$ PEI U/mL, mean (SD)	2.0 (0.3)	2.5 (0.3)	2.6 (0.8)	-
HBcrAg, $\log_{10}$ U/mL, mean (SD)	8.0 (1.2)	8.3 (0.5)	8.3 (0.6)	3.3 (0.6)
ALT, U/L, mean (SD)	38.7 (9.1)	41.5 (22.7)	60.7 (36.9)	35.0 (14.5)

PEVY – pevifoscorvir sodium

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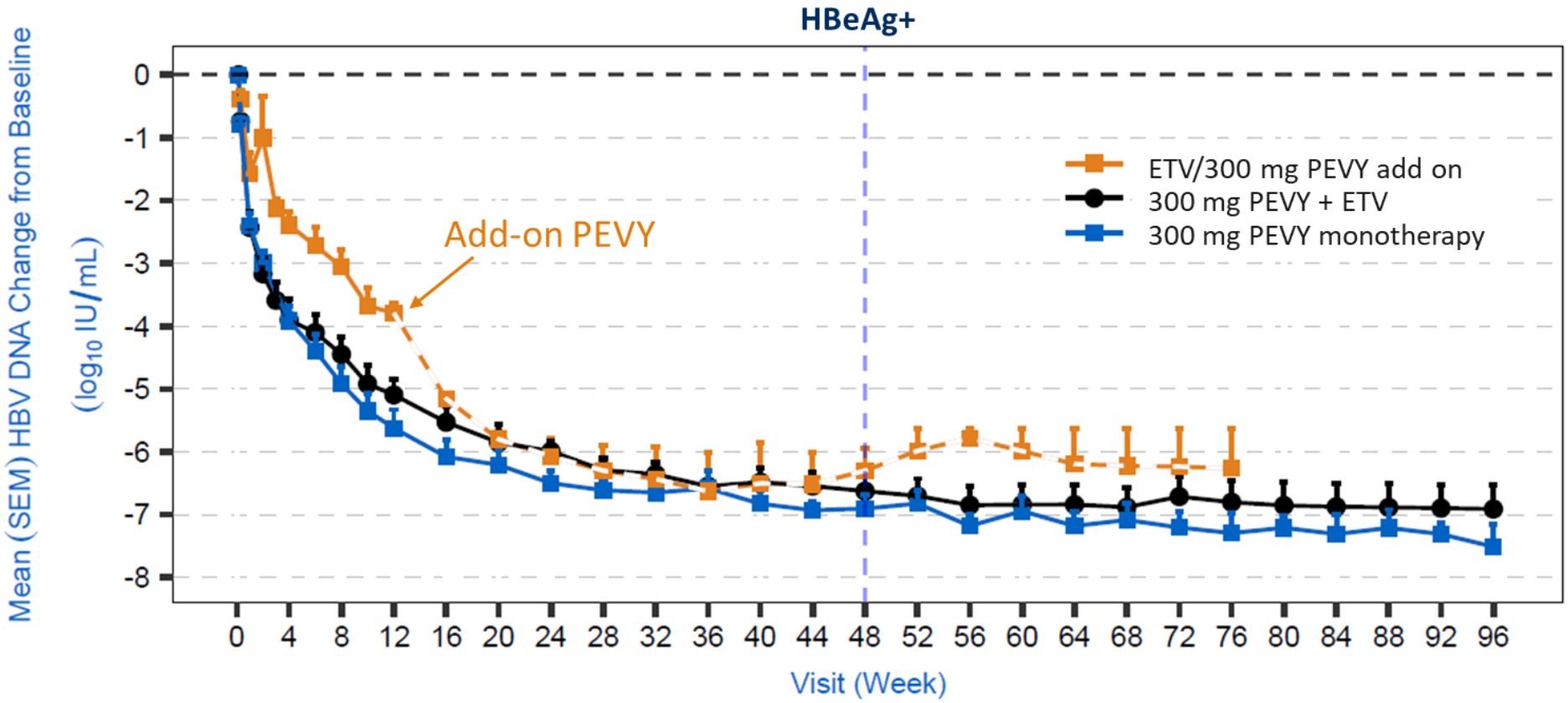
300 mg Pevifoscorvir Sodium ± ETV in HBeAg Positive Subjects

Mean HBV DNA Change from Baseline



ETV/300 mg PEVY add on	3	3	3	3	3	2	2			
300 mg PEVY + ETV	11*	9	9	9	8	8	7	7	7	
300 mg PEVY monotherapy	10	10	10	10	10	10	10	10	10	

Source: Study ALG-000184-201; *one subject excluded due to dosing non-compliance; PEVY – pevifoscorvir sodium

300 mg pevifoscorvir sodium demonstrates greater HBV DNA reduction than ETV monotherapy

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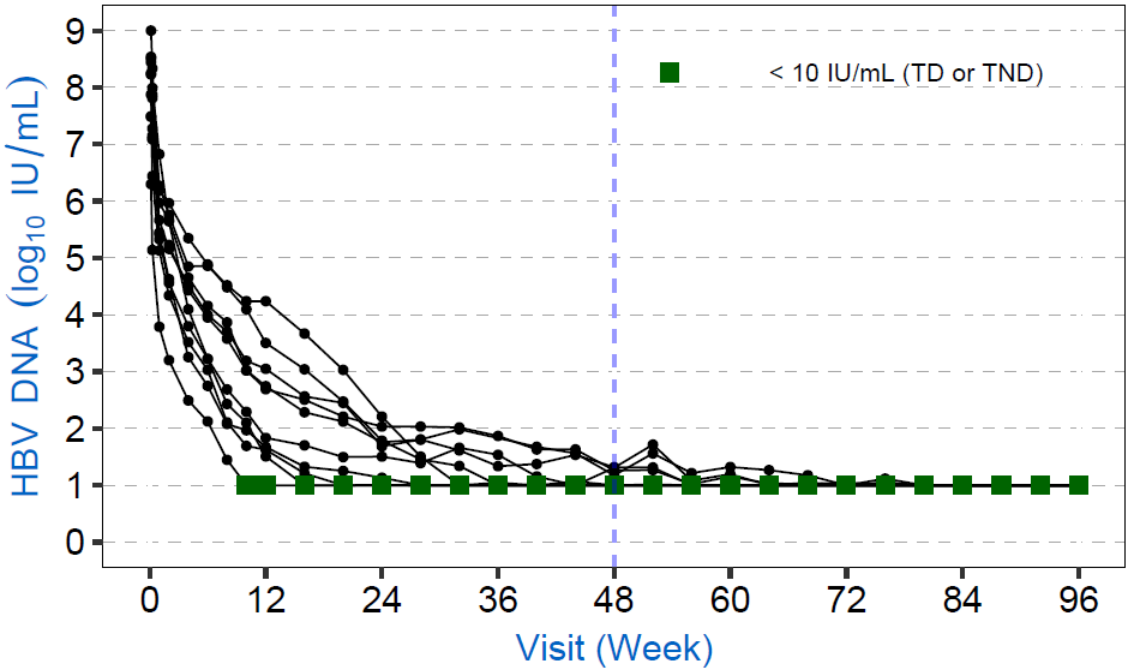
300 mg Pevifoscorvir Sodium Monotherapy

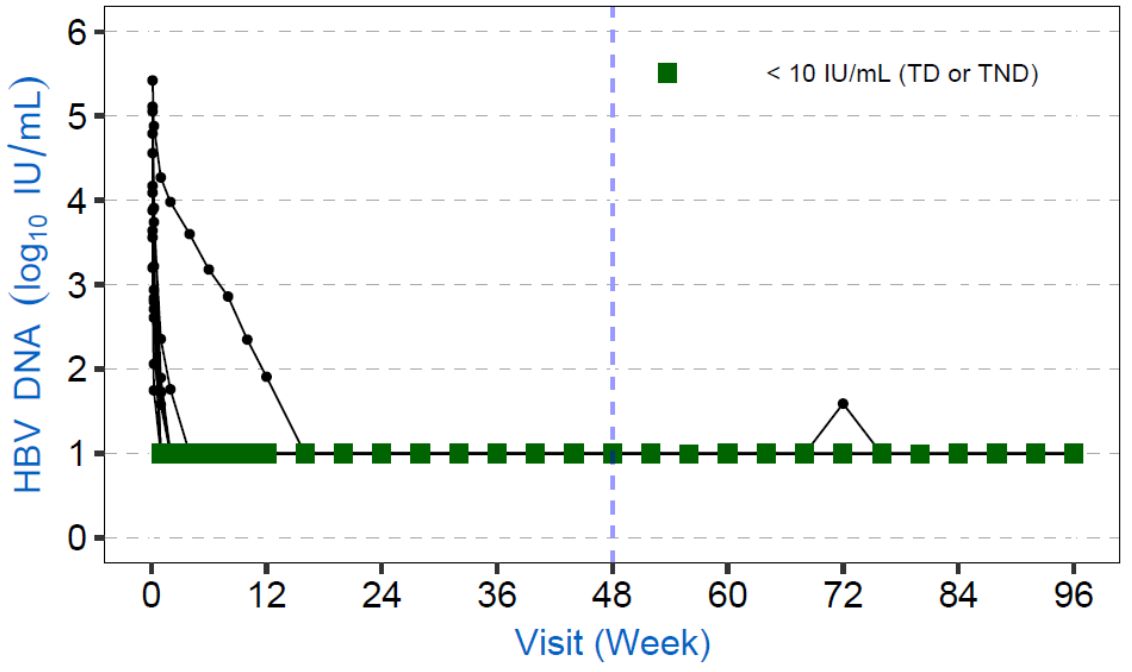
Reduction in Individual HBV DNA Level Over Time

HBeAg+



Total n	10	10	10	9	10	10	10	10	10
< 10 IU/mL (TD or TND)	0	1	2	5	6	7	9	10	10
< 10 IU/mL (TND)	0	0	0	0	0	0	2	3	5

HBeAg-



	11	11	11	11	11	10	9	9	9
	0	10	11	11	11	10	8	9	9
	0	7	6	7	10	8	7	8	8

Source: Study ALG-000184-201.TD – target detected; TND – target not detected, LOD ≤ 4.29 IU/mL

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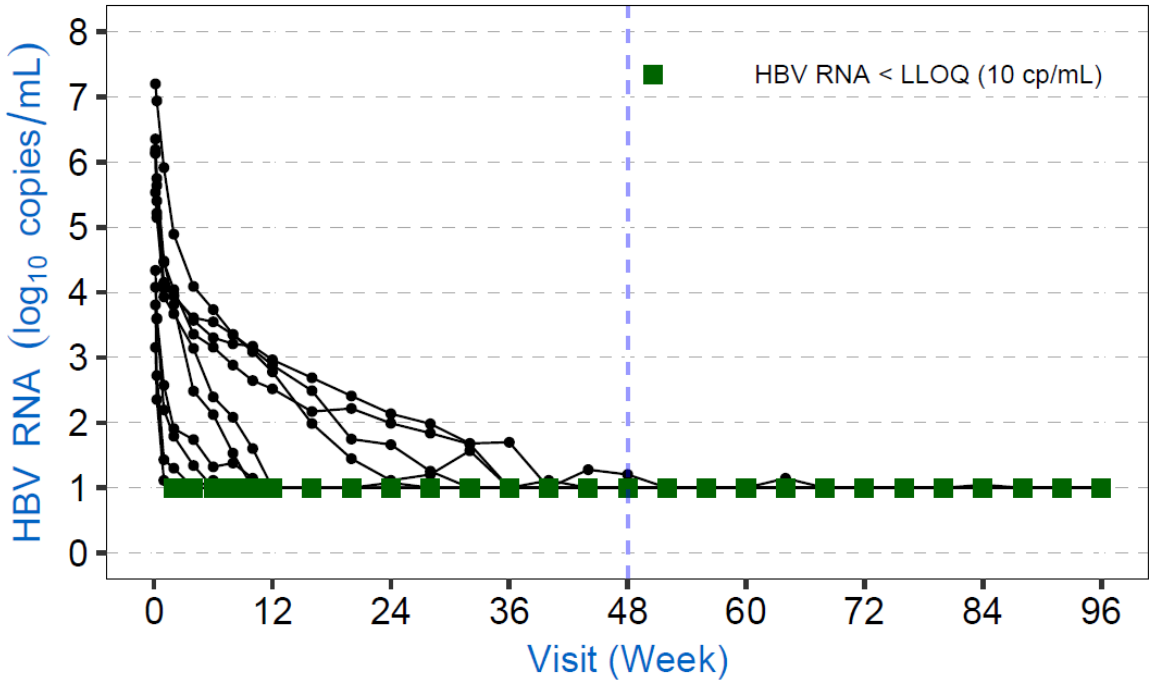
300 mg pevifoscorvir sodium monotherapy demonstrates profound HBV DNA reduction in TN/CNT subjects with chronic HBV infection; no viral breakthrough observed

300 mg Pevifoscorvir Sodium Monotherapy

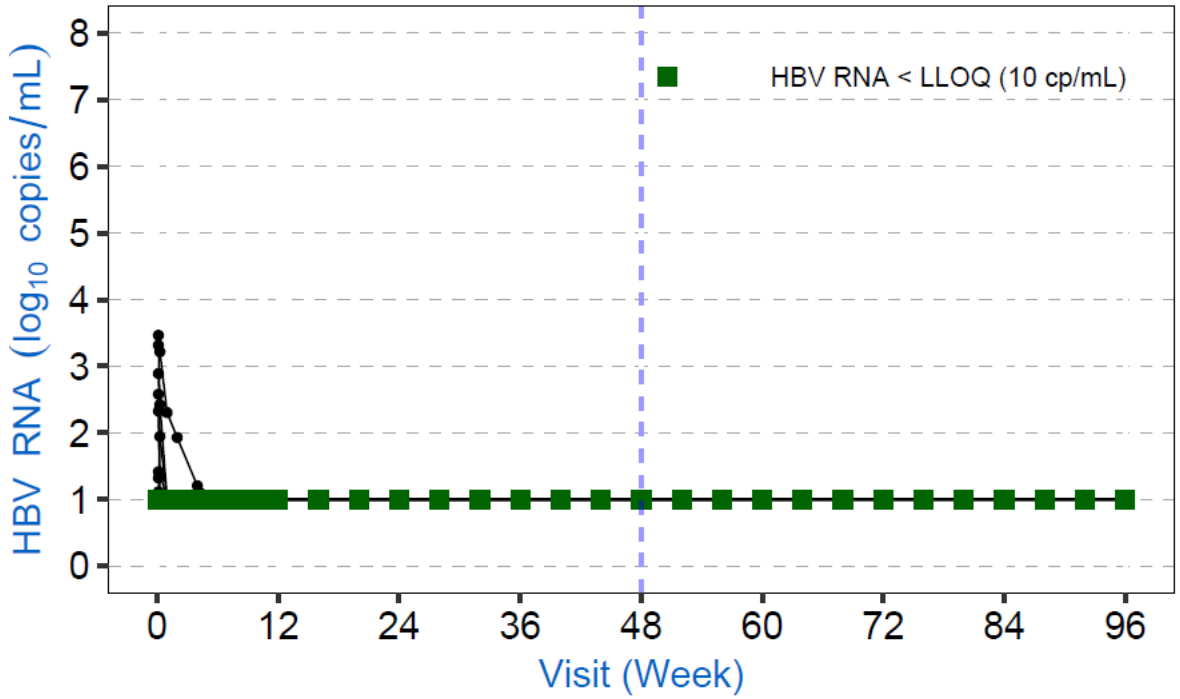
Reduction in Individual HBV RNA Level Over Time

HBeAg+



Total n	10	10	10	9	10	10	10	10	10
< 10 cp/mL	0	6	5	8	9	10	10	9	10

HBeAg-



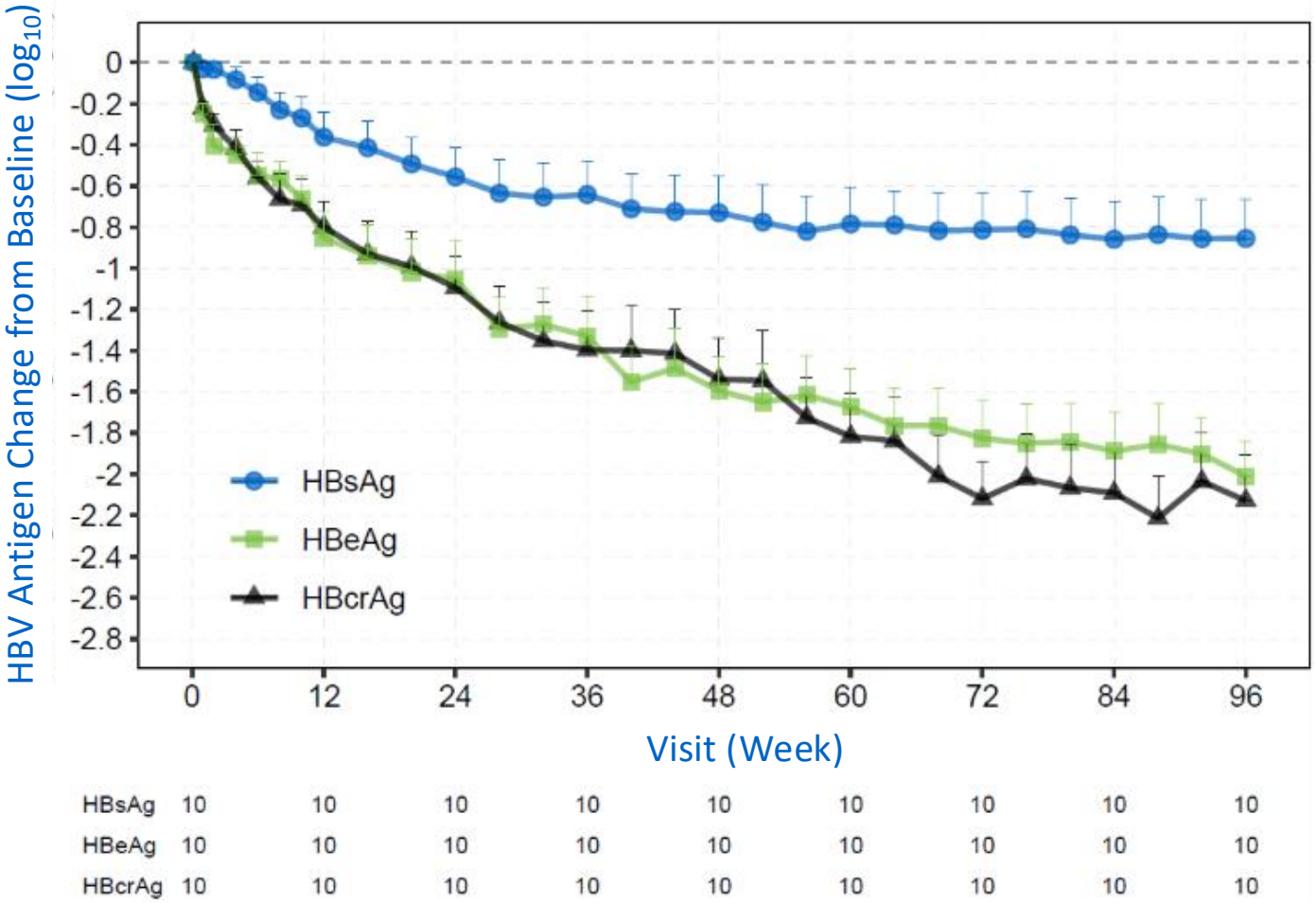
	11	11	11	11	11	10	9	9	9
	3	11	11	11	11	10	9	9	9

Source: Study ALG-000184-201. LLOQ – lower limit of quantitation, cp - copies.

300 mg pevifoscorvir sodium monotherapy demonstrates a rapid and profound HBV RNA reduction in TN/CNT subjects with chronic HBV infection

300 mg Pevifoscorvir Sodium Monotherapy in HBeAg Positive Subjects

Mean HBV Antigen Change From Baseline



Note: Data represents Mean (SEM) at each visit. Source: Study ALG-000184-201.

Substantial HBsAg, HBeAg, and HBcrAg reductions noted in HBeAg+ subjects

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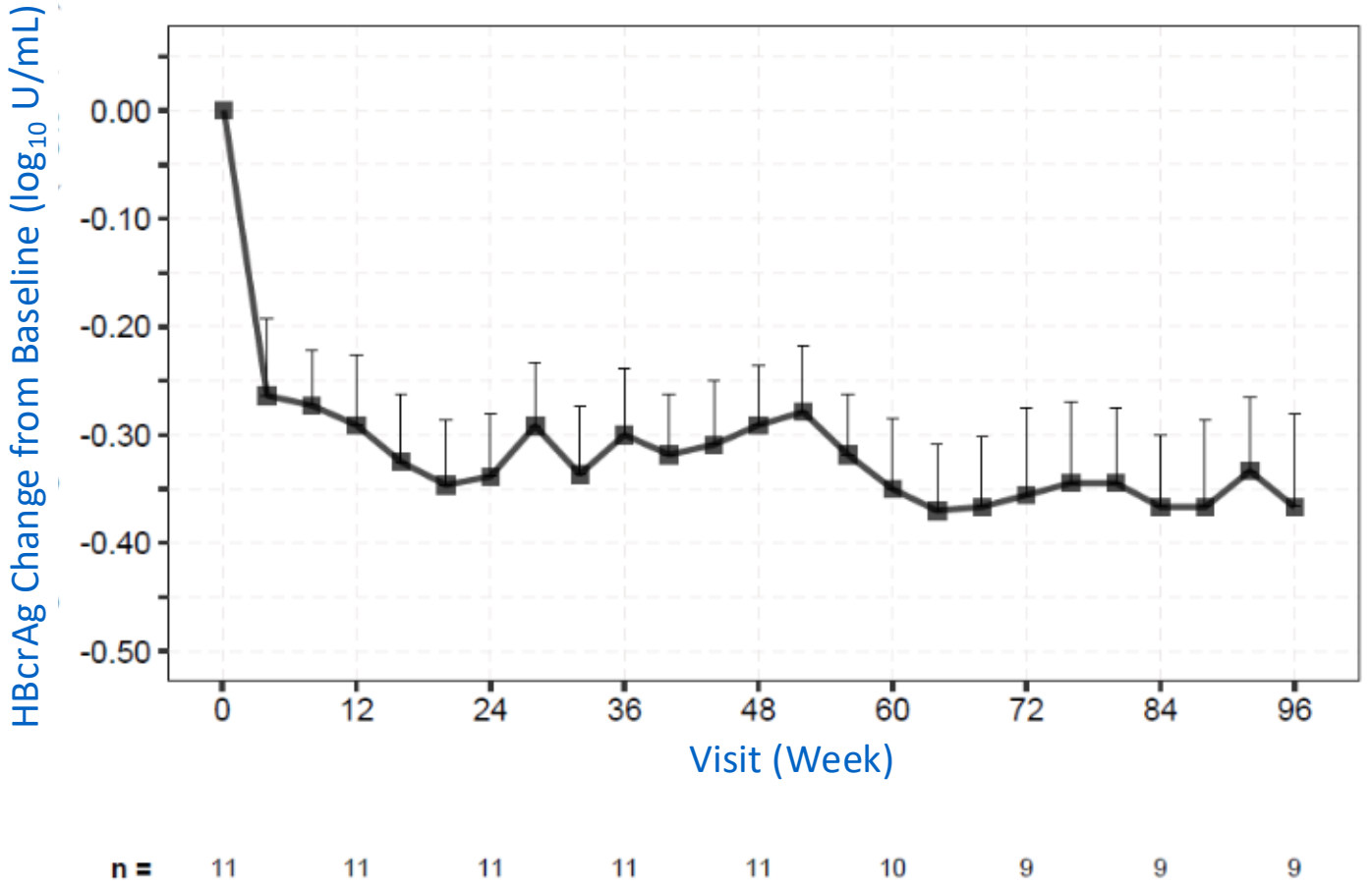
300 mg Pevifoscorvir Sodium Monotherapy in HBeAg Negative Subjects

Mean HBcrAg Change From Baseline



Note: Data represents Mean (SEM) at each visit. Source: Study ALG-000184-201.

Meaningful HBcrAg reduction in HBeAg- subjects, no change in HBsAg

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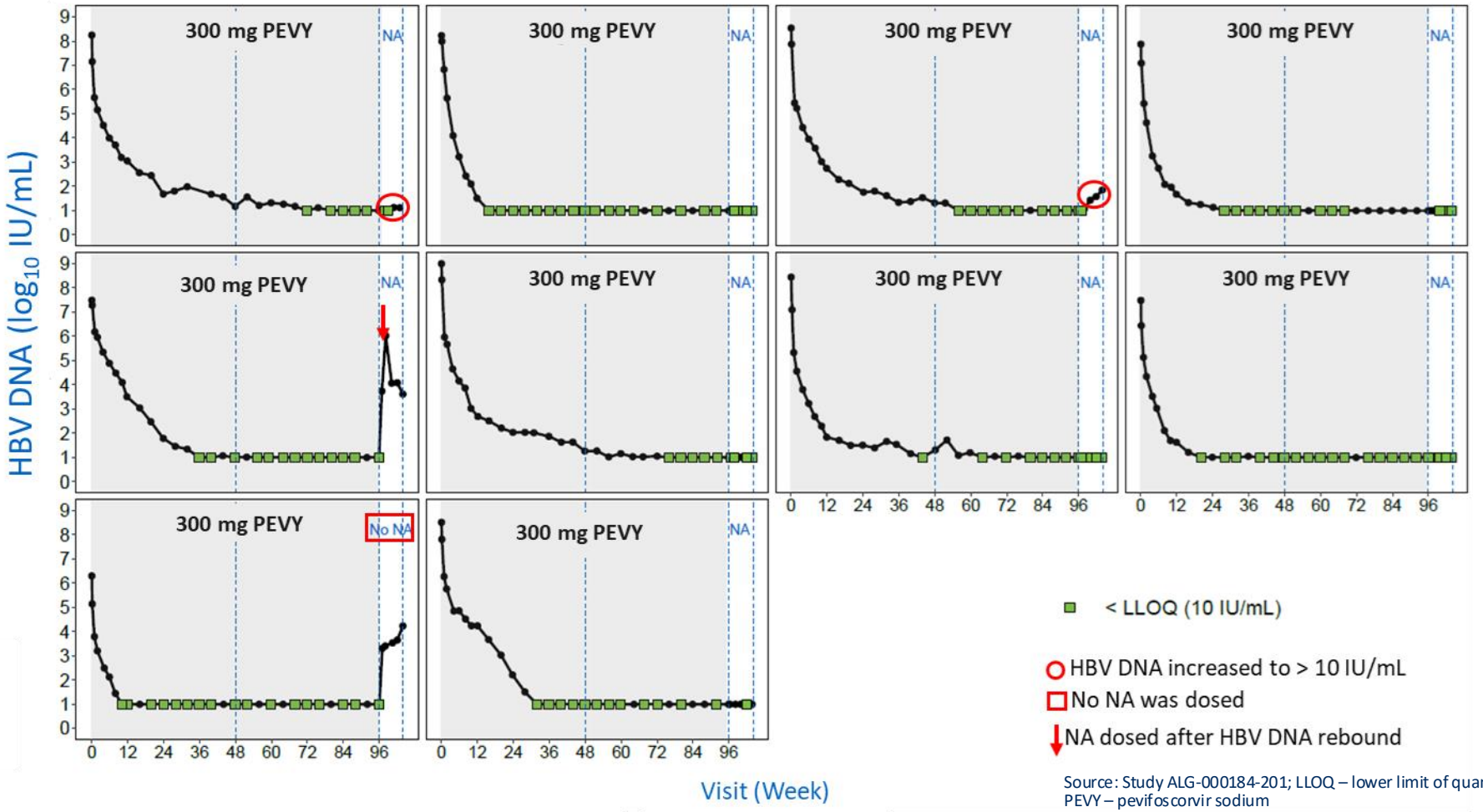
300 mg Pevifoscorvir Sodium Monotherapy in HBeAg Positive Subjects

Individual HBV DNA Change from Baseline Including NA only 8-Week Follow-Up



Source: Study ALG-000184-201; LLOQ – lower limit of quantitation; PEVY – pevifoscorvir sodium

8/10 HBeAg+ subjects switched to NA monotherapy at Week 96
(2 subjects had HBV DNA level > 10 IU/mL during the NA only 8 Week follow-up)

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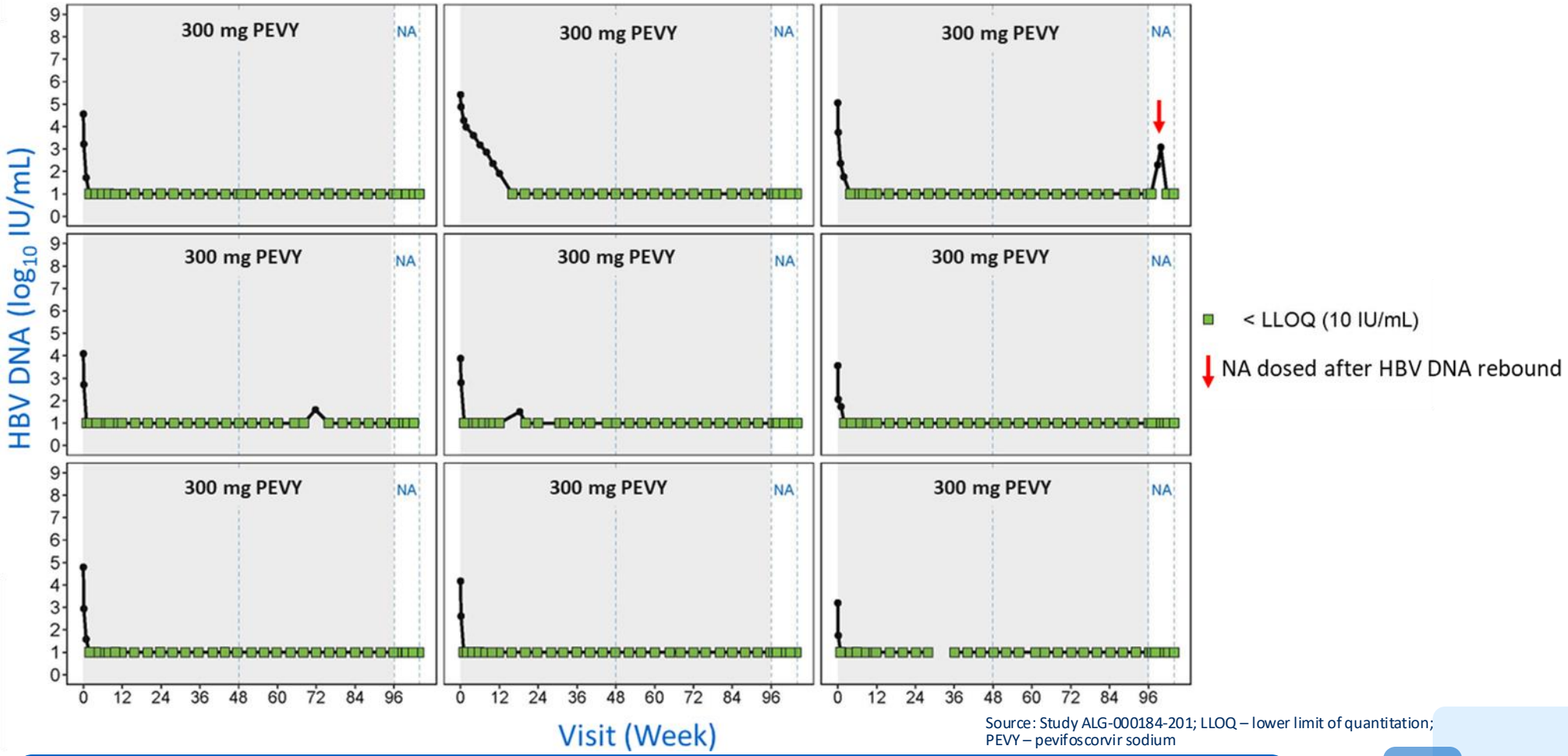
300 mg Pevifoscorvir Sodium Monotherapy in HBeAg Negative Subjects

Individual HBV DNA Change from Baseline Including NA only 8-Week Follow-Up



Source: Study ALG-000184-201; LLOQ – lower limit of quantitation; PEVY – pevifoscorvir sodium

8/9 HBeAg- subjects switched to NA monotherapy at Week 96
(all 8 HBV DNA level < 10 IU/mL during NA only 8 Week follow-up)

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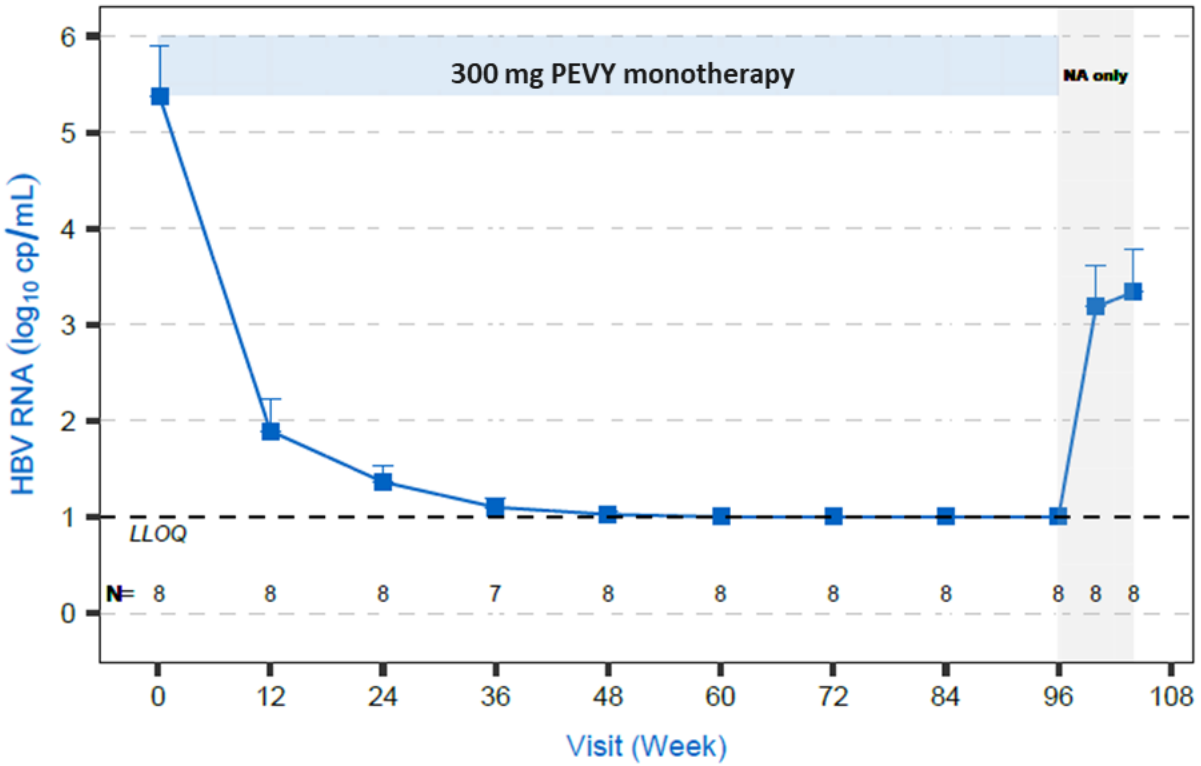
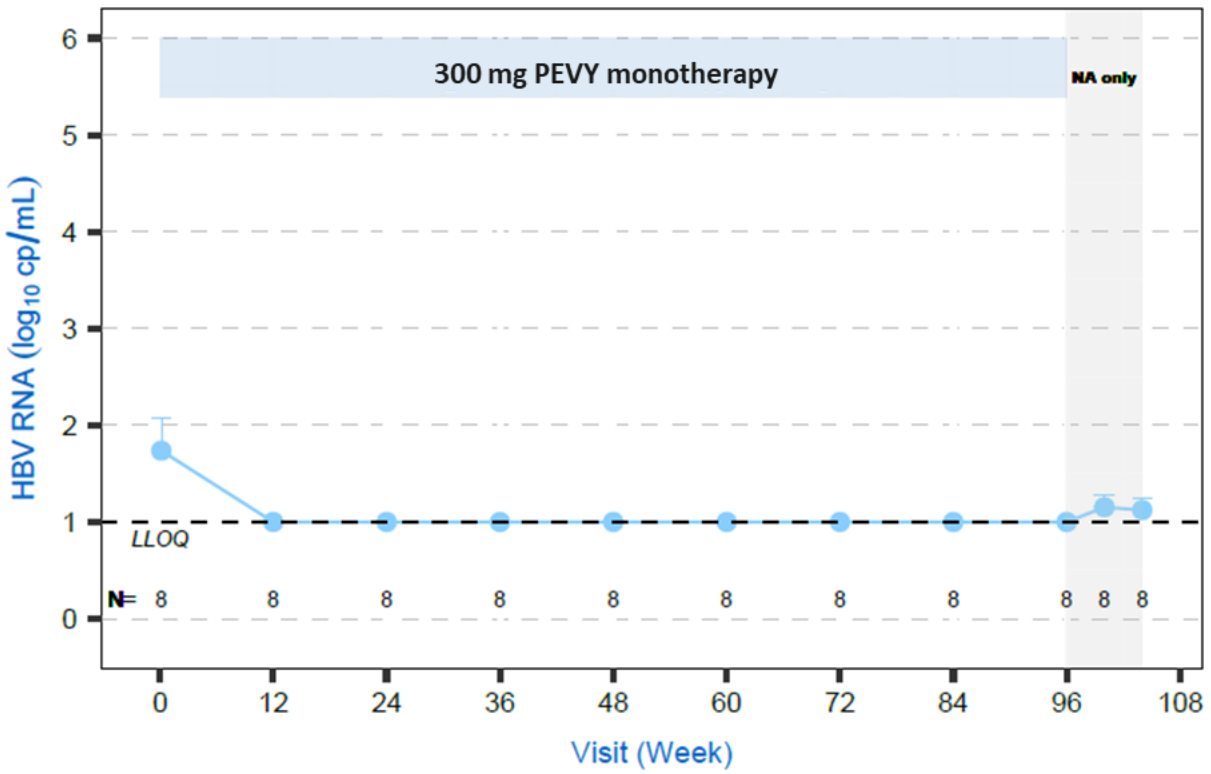
300 mg Pevifoscorvir Sodium Monotherapy

Mean HBV RNA Level Including NA only 8-Week Follow-Up

HBeAg+



HBeAg-



Note: only included subjects who completed 96 weeks of treatment and received NA from W96 through follow up;
PEVY – pevifoscorvir sodium

HBV RNA rebounds after switching to NA but remains lower than baseline

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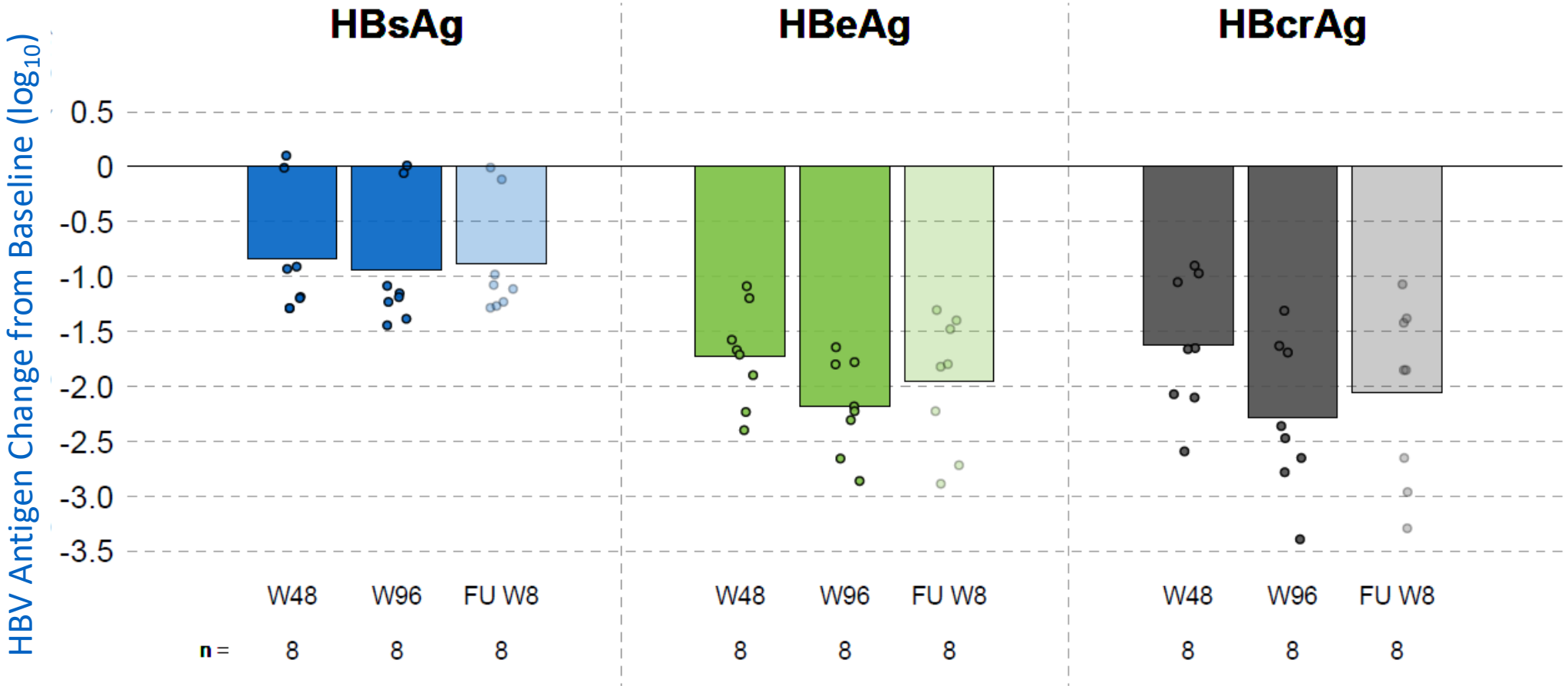
300 mg Pevifoscorvir Sodium in HBeAg Positive Subjects

Mean HBV Antigen Change From Baseline Including NA Only 8-Week Follow-Up



Note: Data represent Mean and individual decline at each visit . FU-follow-up, W-Week;
Source: Study ALG-000184-201.

No apparent increase in HBV antigens during the NA only 8 Week follow-up

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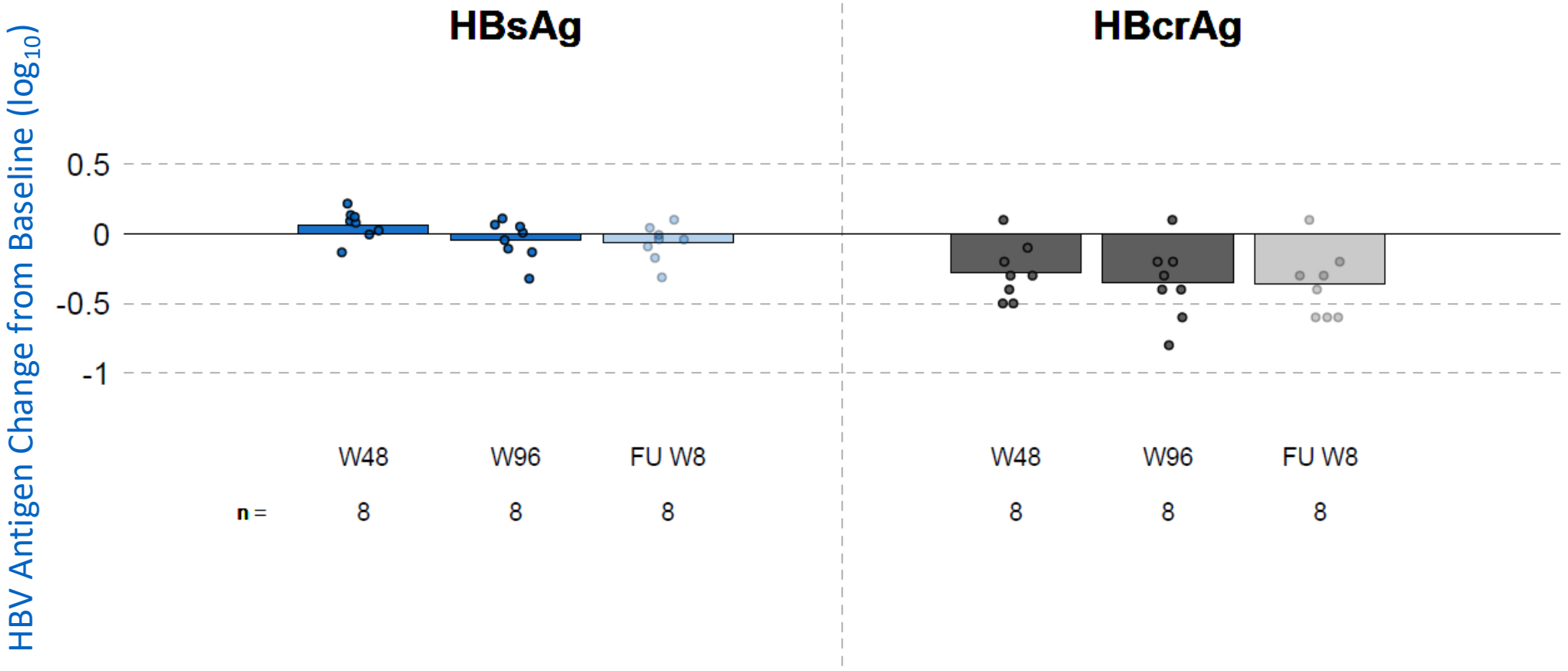
300 mg Pevifoscorvir Sodium Monotherapy in HBeAg Negative Subjects

Mean HBV Antigen Change From Baseline Including NA Only 8-Week Follow-Up



Note: Data represent Mean and individual decline at each visit. FU-follow-up;
Source: Study ALG-000184-201.

HBcrAg decline was maintained during the NA only 8 Week follow-up

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96-Week 300 mg Pevifoscorvir Sodium Monotherapy Post Treatment Data

8-Week NA Follow Up

HBeAg Status	Viral Marker	Data
E-	HBV DNA	8/8 subjects had HBV DNA level < 10 IU/mL during NA only 8 Week follow-up
	HBV RNA	HBV RNA rebounds slightly after switching to NA but remains lower than baseline
	HBV Antigens	HBcrAg decline was maintained during the NA only 8 Week follow-up
E+	HBV DNA	6/8 subjects had HBV DNA level < 10 IU/mL during the NA only 8 Week follow-up
	HBV RNA	HBV RNA rebounds after switching to NA but remains lower than baseline
	HBV Antigens	No apparent HBV antigens increase observed during the NA only 8 Week follow-up

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These data suggest that pevifoscorvir sodium may reduce the cccDNA pool through engagement of its secondary mechanism of action

300 mg Pevifoscorvir Sodium Monotherapy

Safety Following 96 Weeks of Treatment

	HBeAg+	HBeAg-
Numbers of subjects with	N=10	N=11^
• **At least one TEAE, n (%)**	9 (90)	9 (81.8)
• **SAE**	0	0
• **TEAE leading to study drug discontinuation**	0	0
• **TEAE Grade ≥3**	3*	2*,#

^ Two HBeAg-negative subjects withdrew at Week 56 and 64 due to non-safety personal decisions.
* Grade ≥3 TEAEs of ALT/AST elevation were observed in 3 HBeAg-positive and 1 HBeAg-negative subjects with preserved synthetic and excretory functions. All events resolved in the setting of continued pevifoscorvir sodium dosing and were not considered clinically concerning by the ALT Flare Committee.
# Grade 3 cholesterol/triglycerides increase in HBeAg-negative subject resolved in the setting of continued pevifoscorvir sodium dosing.

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Favorable safety profile observed in TN/CNT HBeAg+ and HBeAg- subjects with chronic HBV infection who received 300 mg pevifoscorvir sodium monotherapy for 96 weeks

Summary

Pevifoscorvir Sodium 300 mg Monotherapy for 96 Weeks

- Pevifoscorvir sodium 300 mg monotherapy in TN/CNT HBeAg+ and HBeAg- subjects for 96 weeks demonstrated:
  - Favorable safety profile
  - Rapid, profound and durable reduction in HBV DNA without viral breakthrough
    - In HBeAg-positive subjects, 60% subjects achieved HBV DNA level < 10 IU/mL at Week 48, and increased to 100% at Week 96
    - In HBeAg-negative subjects, 100% achieved HBV DNA < 10 IU/mL by Week 20 and 89% (8/9) achieved < LOD (≤ 4.29 IU/mL) at Week 96
  - Rapid and profound reduction in HBV RNA
  - Multiple log reduction in HBV antigens were achieved
- HBV antigen and HBV RNA reduction were maintained during NA only 8-Week follow up suggesting pevifoscorvir sodium potentially reduces cccDNA pool due to engagement of the CAM-E secondary MOA
- The Phase 2, B-SUPREME study (NCT06963710) evaluating 300 mg pevifoscorvir sodium monotherapy compared to NA monotherapy in TN/CNT subjects with chronic HBV infection, including liver biopsy sub-study, is currently ongoing

Study ALG-000184-201.TD-target detected, TND-target not detected, TN-treatment naïve, CNT-currently not treated.

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