Efficacy of Elebsiran (VIR-2218) and Tobevibart (VIR-3434) in Participants with Chronic Hepatitis Delta Infection: Patterns of HDV RNA Responses through Week 96

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Background

- Chronic hepatitis delta infection causes the most severe form of chronic viral hepatitis and has limited approved treatment options[1]
- Approximately 7 million active viremic patients worldwide, with an average progression to cirrhosis and liver failure of 5 years[2,3]
- Achieving HDV RNA target not detected (TND) may be associated with long-term clinical outcome improvement and lower risk of off-treatment relapse[4]
- Previously reported Week 96 results from the ongoing Phase 2 SOLSTICE study showed high rates of HDV RNA TND and reductions in ALT and HBsAg with monthly elebsiran and tobevibart, an investigational combination therapy for the treatment of chronic HDV infection[5,6]
- Here, we present patterns of HDV RNA responses in participants receiving 96 weeks of monthly elebsiran and tobevibart combination therapy

ALT, alanine aminotransferase; HBsAg, hepatitis B surface antigen; HDV, hepatitis D virus; TND, target not detected.

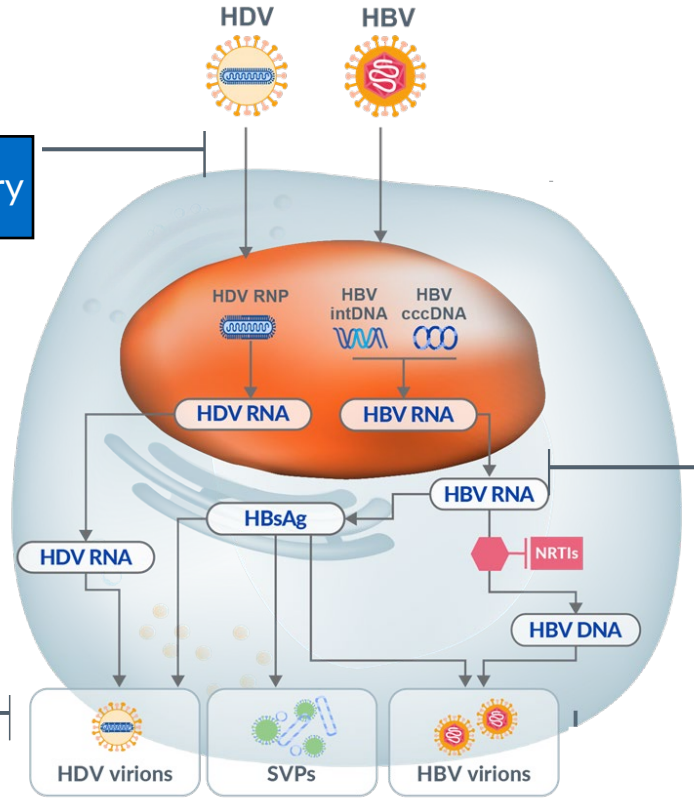
1. World Health Organization. Hepatitis D. July 2026. Accessed August 27, 2026. https://www.who.int/news-room/fact-sheets/detail/hepatitis-d. 2. Stockdale AJ, et al. *J Hepatol*. 2020;73(3):523-532. 3. Pan C, et al. Dig Dis Sci. 2023;68(8):3237-3248. 4. Wedemeyer H, et al. *J Hepatol*. 2026;85(3):493-503. 5. Asselah T, et al. *N Engl J Med*. 2026;394:343-353. 6. Asselah T, et al. *EASL*. May 2026.

Elebsiran and Tobevibart Mechanisms of Action

Tobevibart

(mAb)

Inhibiting viral entry



Elebsiran

(siRNA)

Degrading HBV mRNA & reducing HBsAg production

Neutralizing HDV & HBV virions

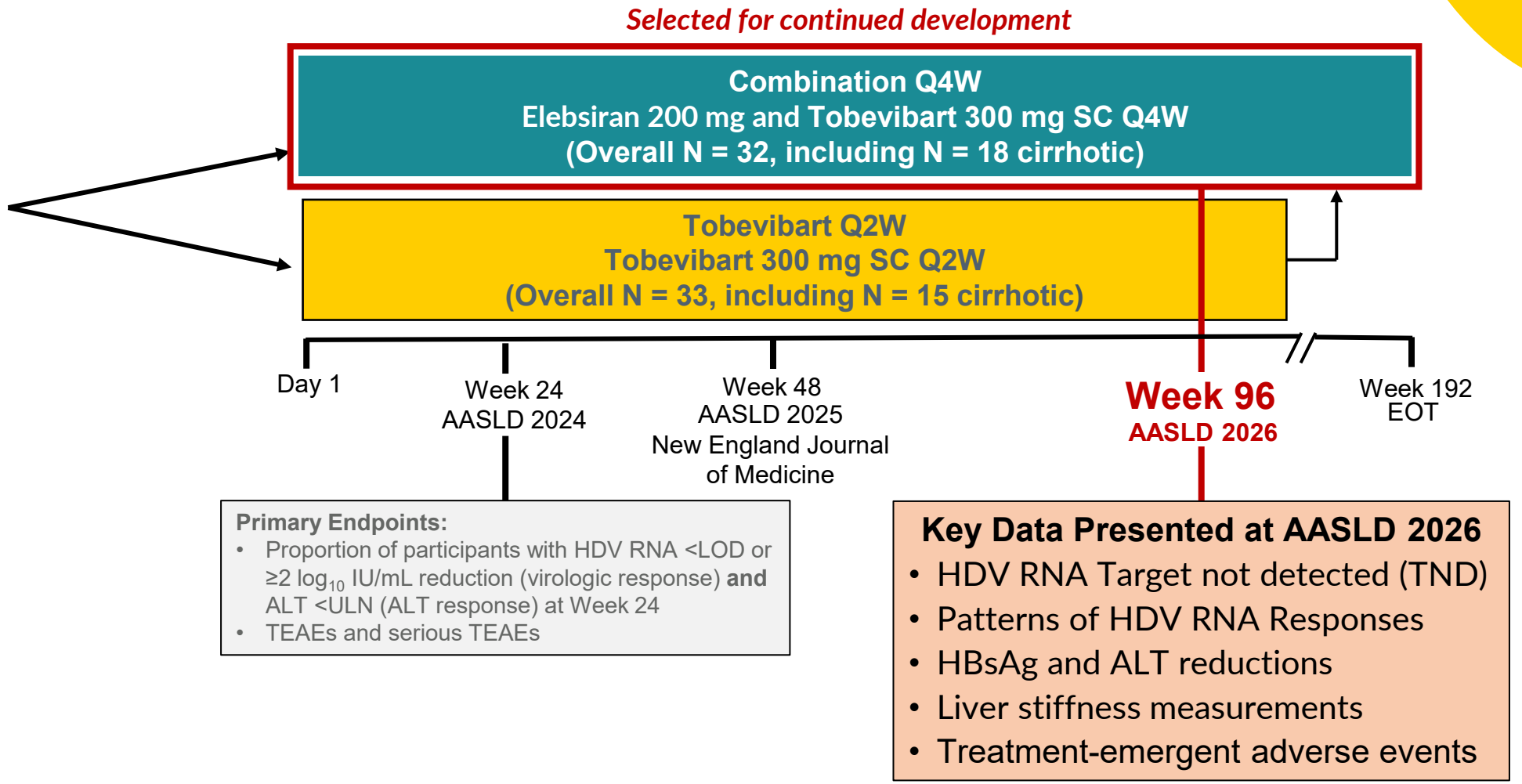
Elebsiran, an siRNA, and tobevibart, a mAb, have complementary mechanisms of action against HDV and HBV

cccDNA, covalently closed circular DNA; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HDV, hepatitis D virus; intDNA, integrated DNA; mAb, monoclonal antibody; mRNA, messenger RNA; NRTI, nucleos(t)ide reverse transcriptase inhibitor; RNP, ribonucleoprotein; siRNA, small interfering RNA; SVP, subviral particle.

SOLSTICE Simplified Study Design: Elebsiran and Tobevibart Q4W and Tobevibart Q2W in Participants Living with Chronic HDV Infection

HDV RNA >500 IU/mL
ALT >ULN; ALT <5 × ULN
Non-cirrhotic[a]
or cirrhotic (CTP-A)[b]
N = 65, randomized 1:1

All participants remained on concomitant NA therapy throughout the duration of the study.



SOLSTICE ClinicalTrials.gov Identifier: NCT05461170.
ALT, alanine aminotransferase; CTP, Child-Turcotte-Pugh; EOT, end of treatment; HDV, hepatitis D virus; LOD, limit of detection; NA, nucleos(t)ide analogue; Q2W, once every 2 weeks; Q4W, once every 4 weeks; SC, subcutaneous; TEAE, treatment-emergent adverse event; ULN, upper limit of normal.
HDV RNA was measured using RoboGene 2.0 with manual RNA extraction; HDV RNA LLOQ = 63 IU/mL; HDV RNA LOD = 14 IU/mL.
[a]Non-cirrhotic: liver biopsy with METAVIR F0 to F3 or liver stiffness <12 kPa within 12 months of screening and platelet count >150 × 10^3/μL.
[b]Compensated cirrhotic participants: liver biopsy with METAVIR F4 or liver stiffness ≥12 kPa within 12 months of screening, a platelet count >90 × 10^3/μL, and a CTP score of 5 or 6, inclusive at screening and at the start of the study.

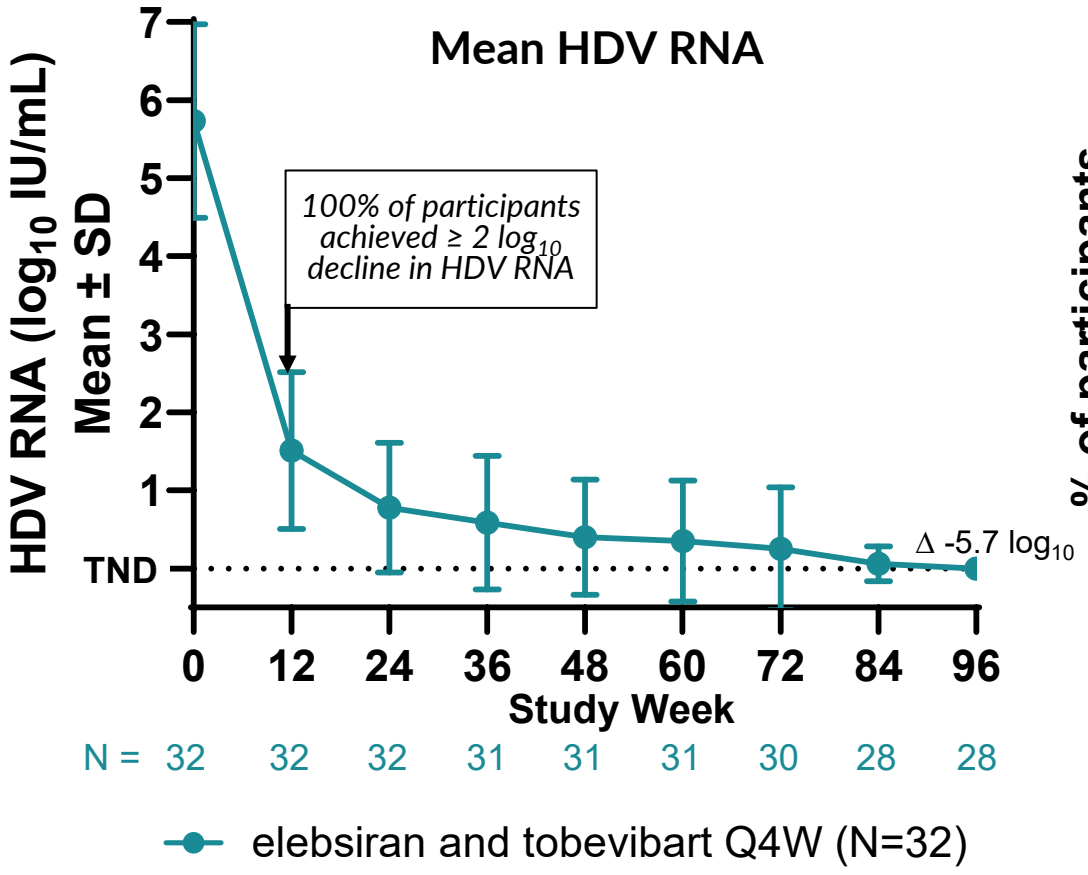
Participant Demographics and Baseline Characteristics

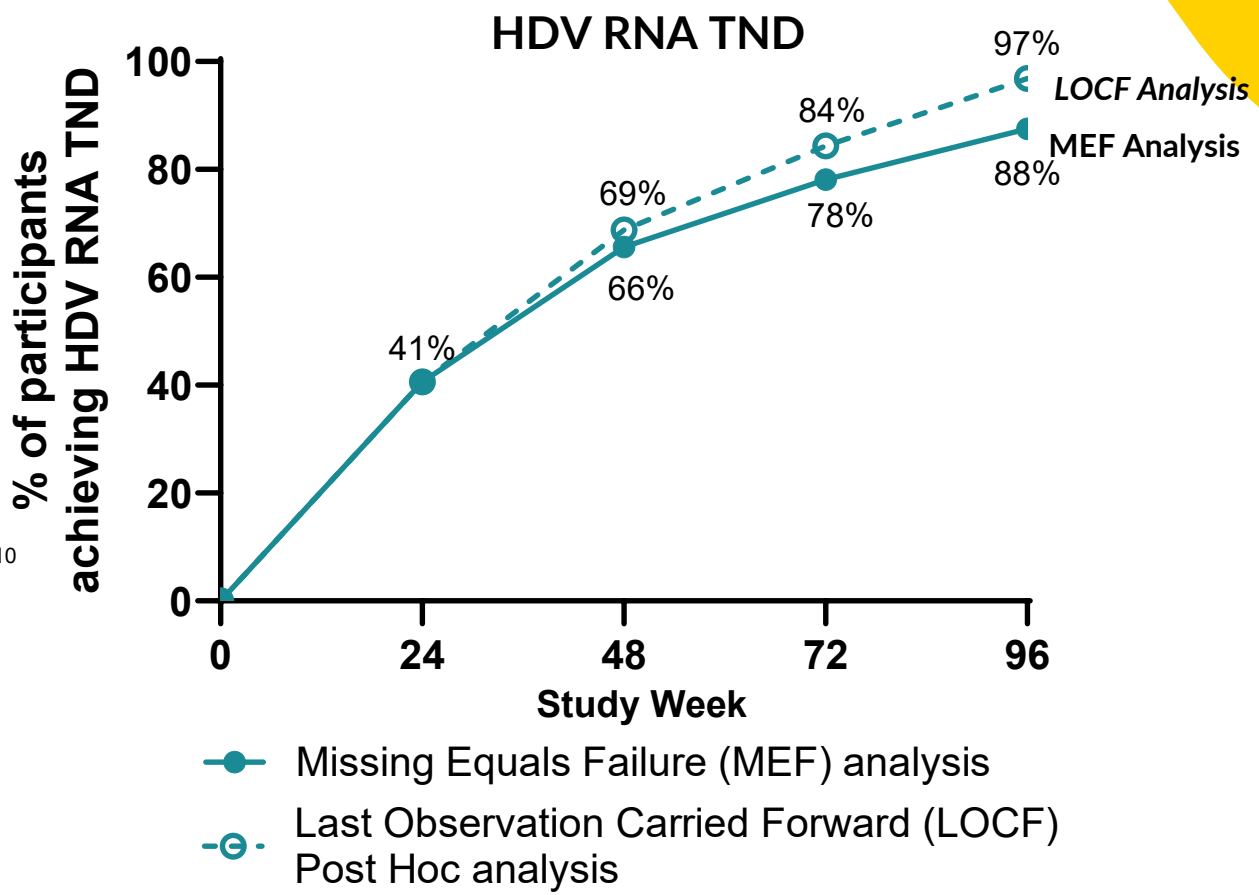
	Elebsiran and tobevibart Q4W N = 32
Age, y, mean ± SD	41.5 ± 8.0
Male, n (%)	18 (56.3)
Race, n (%)	
White	25 (78.1)
Black or African American	4 (12.5)
Asian	2 (6.3)
Other	1 (3.1)
ALT, U/L, mean ± SD	83.4 ± 47.1
HDV RNA, log_{10} IU/mL, mean ± SD	5.7 ± 1.2
HDV genotype, gt (%)	gt1 (97%); gt5 (3%)
HBsAg, log_{10} IU/mL, mean ± SD	3.7 ± 0.6
HBeAg positive, n (%)	3 (9.4)
HBV DNA, log_{10} IU/mL, mean ± SD[a]	0.74 ± 0.66
Cirrhotic participants[b], n (%)	18 (56.3)
Platelets, 10^9/L, mean ± SD	189.4 ± 58.0
Liver stiffness, kPa, mean ± SD	13.5 ± 7.3[c]
FibroTest score, mean ± SD	0.48 ± 0.25

Approximately half of participants enrolled were compensated cirrhotic at baseline.

ALT, alanine aminotransferase; gt, genotype; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HDV, hepatitis D virus; LOD, limit of detection; LLOQ, lower limit of quantification; NA, nucleos(t)ide analogue; Q4W, once every 4 weeks; SD, standard deviation.
HDV RNA was measured using RoboGene 2.0 with manual RNA extraction; HDV RNA LLOQ = 63 IU/mL; HDV RNA LOD = 14 IU/mL.
[a] All participants were on NA therapy at enrollment and remained on concomitant NA therapy throughout the duration of the study; at baseline, 2 participants had HBV DNA >20 IU/mL; the reported mean includes all participants.
[b] Most participants were classified by FibroScan at screening (LSM <12 kPa, non-cirrhotic; ≥12 kPa, compensated cirrhotic); however, a few were classified based on liver biopsy within 12 months prior to enrollment.
[c] 19 participants had baseline liver stiffness ≥10 kPa, including 16 baseline liver stiffness ≥12 kPa and 8 with baseline liver stiffness ≥15 kPa.

Rapid HDV RNA Suppression with Elebsiran and Tobevibart Therapy, with Increasing Rates of HDV RNA TND through Week 96

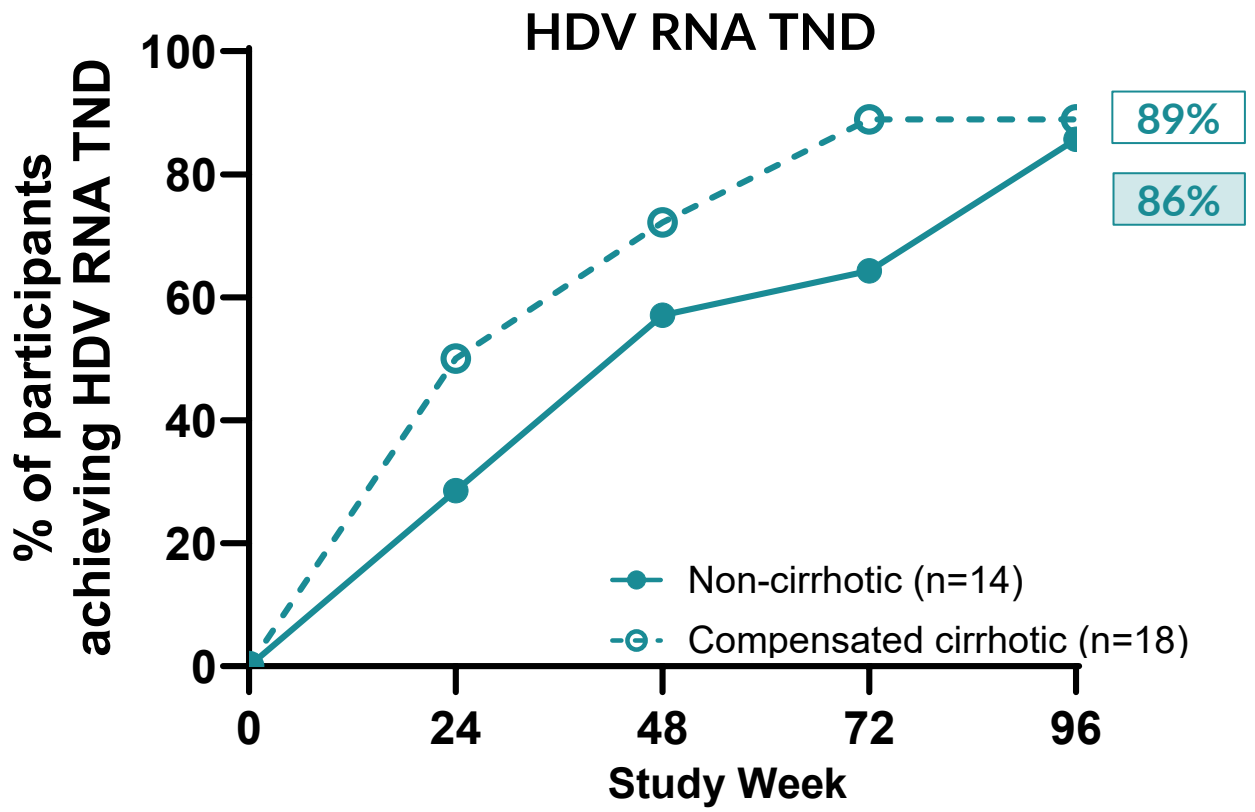




100% of participants had a ≥2 log_{10} decrease in HDV RNA by Week 12 of combo therapy. The proportion with HDV RNA TND increased with continued therapy.

HDV, hepatitis D virus; Q4W, once every 4 weeks; TND, target not detected. HDV RNA TND = undetectable HDV RNA (no amplification during RT-PCR).
*By Week 96, 4 participants in the elebsiran and tobevibart Q4W cohort had discontinued treatment. These participants are counted as failures in the missing equals failure [MEF] analysis or their last observed HDV RNA value was carried forward [LOCF; not pre-specified, post hoc analysis].

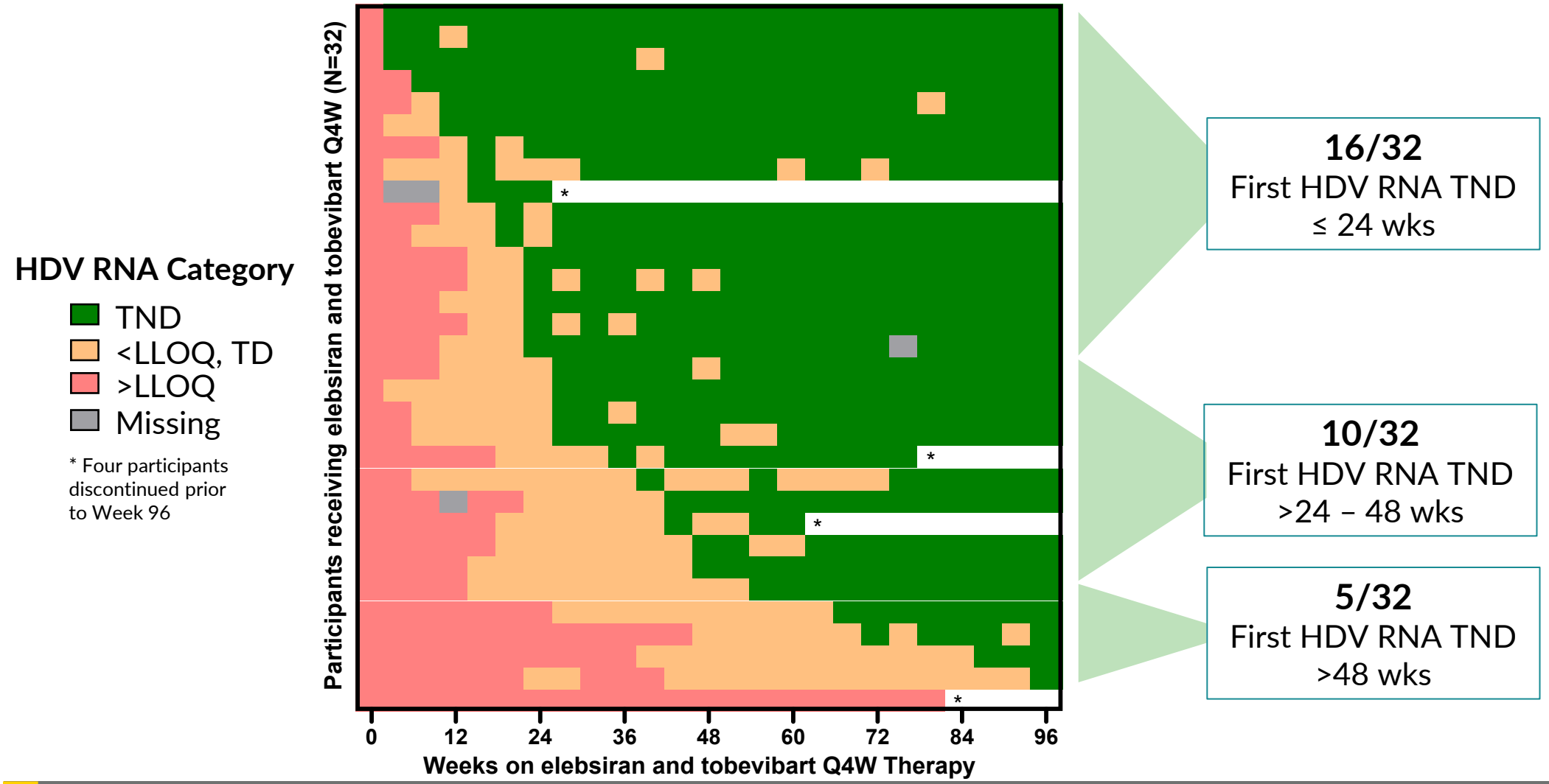
High Rates of HDV RNA TND Were Observed with Elebsiran and Tobevibart Combination Therapy Regardless of Cirrhotic Status



At Week 96, HDV RNA TND was achieved by 89% of compensated cirrhotic and 86% of non-cirrhotic participants treated with elebsiran and tobevibart

HDV, hepatitis D virus; Q4W, once every 4 weeks; TND, target not detected. HDV RNA TND = undetectable HDV RNA (no amplification during RT-PCR).
By Week 96, 4 participants in the elebsiran and tobevibart Q4W cohort had discontinued treatment and are counted as failures in analysis.

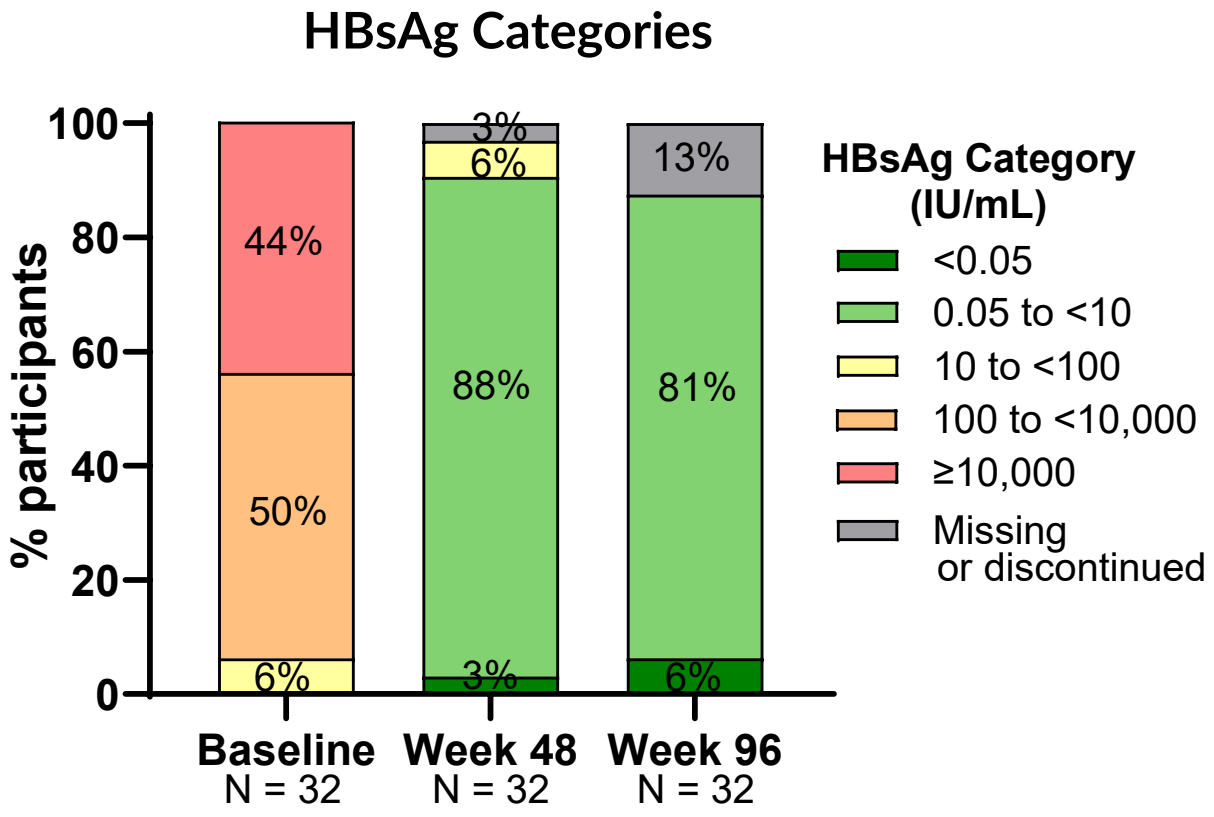
Rapid and Durable HDV RNA Suppression with Elebsiran and Tobevibart

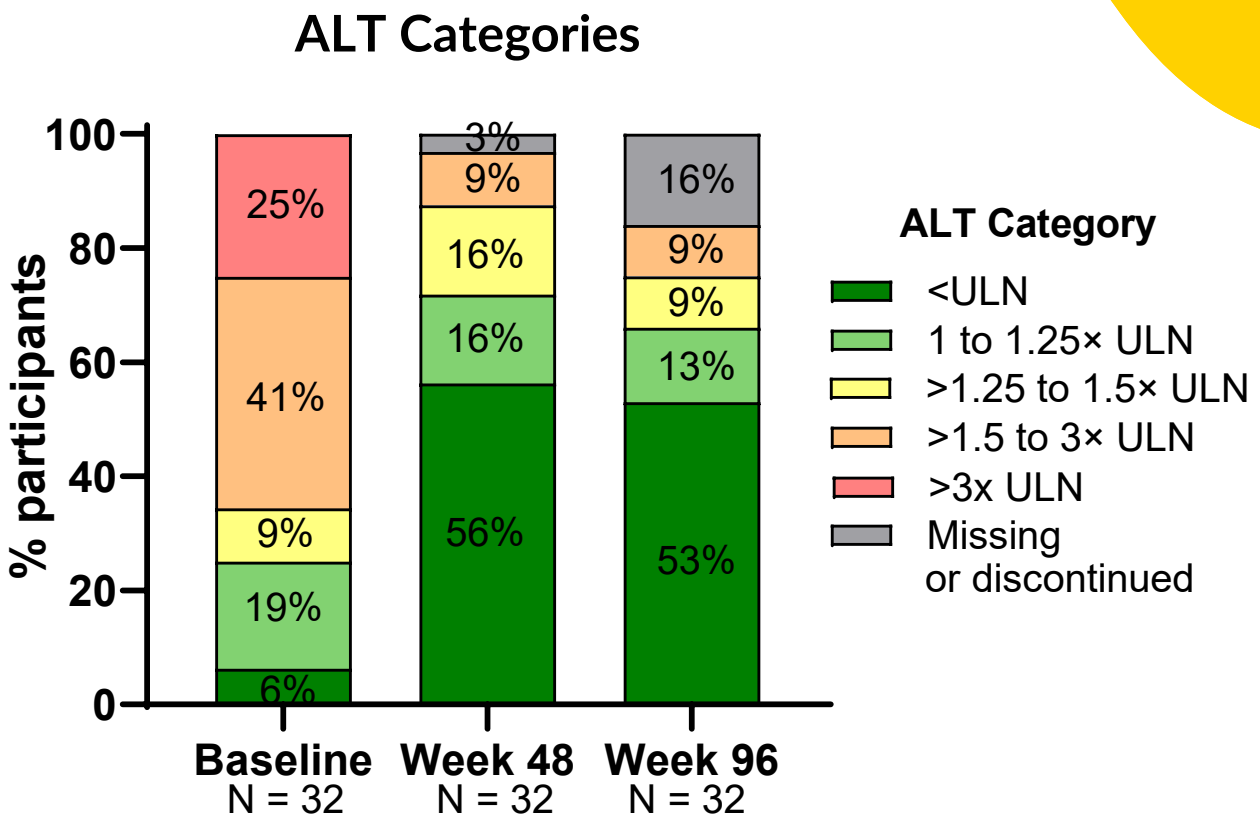


All 28* participants who completed 96 weeks of therapy achieved HDV RNA TND.
Half of participants (16/32) first achieved HDV RNA TND by Week 24.
No HDV RNA rebound >LLOQ was observed after achieving HDV RNA TND on therapy.

HDV, hepatitis D virus; LLOQ, lower limit of quantification; Q4W, once every 4 weeks; TND, target not detected.
HDV RNA assay = RoboGene HDV RNA quantification kit, v2.0; HDV RNA TND = undetectable HDV RNA (no amplification during RT-PCR); LLOQ = 63 IU/mL

Elebsiran and Tobevibart Therapy Reduced HBsAg and ALT



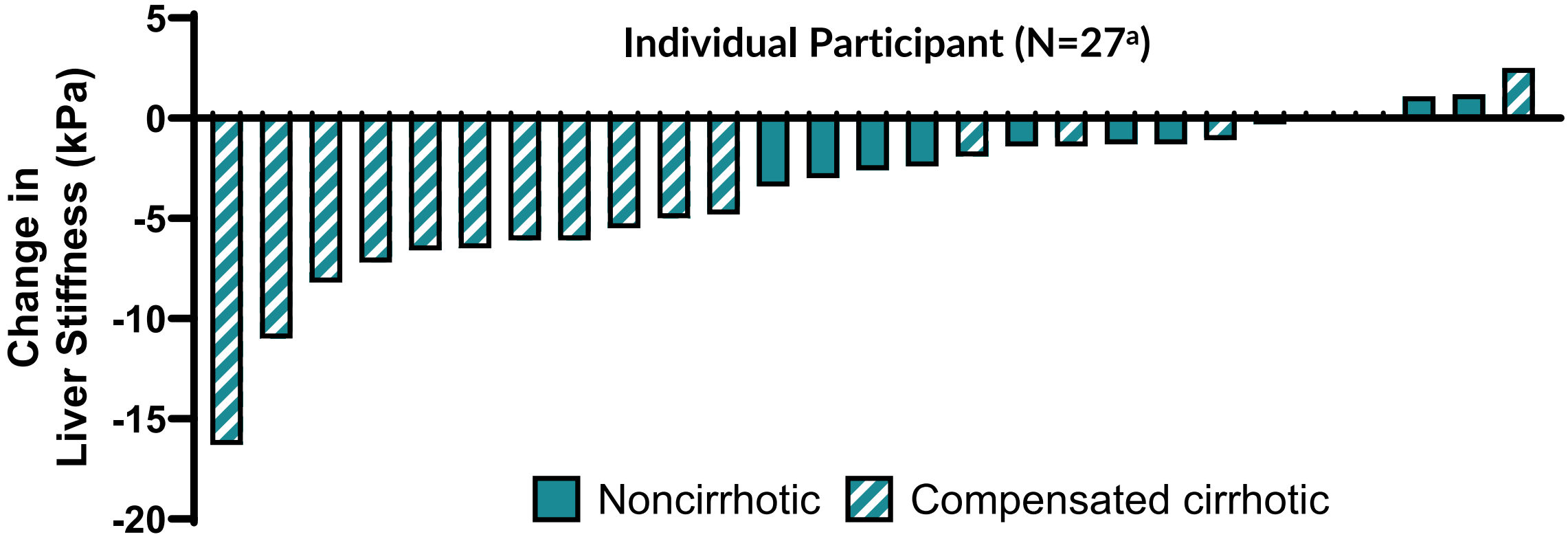


All 28* participants who completed 96 weeks of elebsiran and tobevibart achieved HBsAg <10 IU/mL. At Week 96, 75% of participants achieved ALT ≤1.5× ULN, including 53% with ALT normalization.

ALT, alanine aminotransferase; HBsAg, hepatitis B surface antigen; HDV, hepatitis D virus; Q4W, once every 4 weeks; TND, target not detected. HDV RNA TND = undetectable HDV RNA (no amplification during RT-PCR).
* Four participants discontinued prior to Week 96.

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Most Participants Had Improved or Stable Liver Stiffness Measures after 96 Weeks of Elebsiran and Tobevibart Therapy



Among participants with paired liver stiffness measurements (LSM), 89% showed improved or stable LSM results after 96 weeks.

HDV, hepatitis D virus; TND, target not detected. HDV RNA TND = undetectable HDV RNA (no amplification during RT-PCR).
Liver stiffness measures (LSM), a marker of hepatic inflammation and fibrosis, was measured by Fibroscan.
Participants were classified as noncirrhotic (LSM <12 kPa or METAVIR F0-F3 on liver biopsy within 12 months of screening; platelet count >150 × 10^3/μL) or compensated cirrhotic (LSM ≥12 kPa or METAVIR F4 on liver biopsy within 12 months of screening; CTP-A and platelet count >90 × 10^3/μL).
[a] At Week 96, 2 participants did not have paired a LSM, and 3 participants discontinued without a week 96 LSM.

Majority of Adverse Events Through Week 96 were Grade 1 or 2 and Transient

Safety or tolerability measure, n (%)[a]	Elebsiran and tobevibart Q4W N = 32
Any TEAE	28 (88)
Grade 1-2	27 (84)
Grade 3	1 (3)[b]
Grade 4	0
Treatment-related TEAE	23 (72)
Treatment-emergent injection site reactions[c]	4 (13)
Treatment-emergent flu-like symptoms[d]	17 (53)
Flu-like symptoms reported beyond the 1st dose	1 (3)
TEAE leading to study drug interruption	0
TEAE leading to study drug discontinuation	0
Serious TEAE	1 (3)[e]
Treatment-related serious TEAE	0

There were no study drug-related discontinuations and no related SAEs in participants receiving elebsiran and tobevibart combination therapy.

Q4W, once every 4 weeks; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
[a]A participant with multiple events within a category is counted only once in that category.
[b]Grade 3 worsening of diabetes mellitus type 2 deemed unrelated to study drugs by investigator.
[c]Injection-site reactions included pain, pruritus, erythema, swelling.
[d]Flu-like symptoms are defined as Influenza like illness or chills or any 2 of headache, myalgia, pyrexia, fatigue, arthralgia reported within 7 days after study dosing.
[e]One participant with 2 concurrent SAEs of worsening nasal septum deviation and worsening nasal concha hyperplasia (both Grade 2) who underwent planned admission to the hospital for surgery; both SAEs were deemed unrelated to study drugs by investigator.

Summary of the 28 Participants Completing 96 Weeks of Elebsiran and Tobevibart Combination Therapy

Rapid HDV RNA Suppression	• Half of participants achieved HDV RNA TND by Week 24
Increasing Rates of HDV RNA TND	• All 28 had HDV RNA TND at Week 96[a]
Durable HDV RNA Suppression	• No HDV RNA rebound >LLOQ occurred after achieving TND
Reduction in HBsAg and ALT levels	• All 28 achieved HBsAg <10 IU/mL[a]. • In the full cohort, 53% achieved ALT normalization at Week 96.
Improved or Stable Liver Stiffness Measures	• 89% showed improved or stable LSM results at 96 weeks
Favorable Safety Profile	• Adverse events were generally mild to moderate with no study drug-related discontinuations or SAEs

In conclusion, 96 weeks of elebsiran and tobevibart combination therapy achieved high rates of HDV RNA TND, reductions in ALT and HBsAg, and was generally well tolerated

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HDV, hepatitis D virus; LLOQ, lower limit of quantification; SAE, serious adverse event; TND, target not detected. HDV RNA TND = undetectable HDV RNA (no amplification during RT-PCR).

[a] Four participants discontinued prior to week 96 and are counted as treatment failures in the full cohort analysis.

Elebsiran and tobevibart combination therapy is now being evaluated in a comprehensive registrational program (ECLIPSE studies)

Acknowledgments

- We thank all study participants, site coordinators, and study investigators