Primary Results of ECLIPSE 1: A Randomized Open-Label Phase 3 Study Evaluating Efficacy and Safety of Elebsiran and Tobevibart for Chronic Hepatitis Delta

Nancy Reau,[1] Sophia Chow,[2] Alina Jucov,[3] Saeed Hamid,[4] Zaigham Abbas,[5] Marta Dobryanska,[6] Elena Laura Iliescu,[7] Heiner Wedemeyer,[8] Pietro Lampertico,[9] Carla S. Coffin,[10] Tatyana Kushner,[11] Ed Gane,[12] Kosh Agarwal,[13] Cara Pilowa,[2] Todd Correll,[2] Yimeng Lu,[2] Richard Phan,[2] Michael A. Chattergoon,[2] Tarik Asselah[14]

[1]Rush University Medical Center, Chicago, IL, USA; [2]Vir Biotechnology, Inc., San Francisco, CA, USA; [3]Arensia Exploratory Medicine GmbH, Düsseldorf, Germany, and Nicolae Testemitanu State University of Medicine and Pharmacy, Chişinău, Moldova; [4]Aga Khan University Hospital, Karachi, Pakistan; [5]Ziauddin University Hospital Karachi, Karachi, Pakistan; [6]Arensia Exploratory Medicine, Kyiv, Ukraine; [7]Fundeni Clinical Institute, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [8]Department of Gastroenterology, Hepatology, and Endocrinology, Hannover Medical School, Hannover, Germany; [9]Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [10]Division of Gastroenterology and Hepatology, University of Calgary, Calgary, AB, Canada; [11]Weill Cornell Medicine, New York, New York, USA; [12]Auckland Clinical Studies, Auckland, New Zealand; [13]Institute of Liver Studies, King's College Hospital, London, UK; [14]Université Paris Cité, Hôpital Beaujon (AP-HP), INSERM UMR1149, Paris, France

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Background

- Chronic hepatitis delta infection causes the most severe form of chronic viral hepatitis leading to high rates of cirrhosis, decompensation, and hepatocellular carcinoma[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]
- As previously reported in the SOLSTICE study, elebsiran and tobevibart combination demonstrated reductions in HDV RNA, ALT and HBsAg[5]

Elebsiran and tobevibart combination regimen granted FDA Breakthrough Therapy and Fast Track & EU PRIME Designations

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

1. World Health Organization. Hepatitis D. July 2023. Accessed May 30, 2024. https://www.who.int/news-room/fact-sheets/detail/hepatitis-d. 2. Stockdale A, et al. *J Hepatol*. 2020;73:523-532. 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.

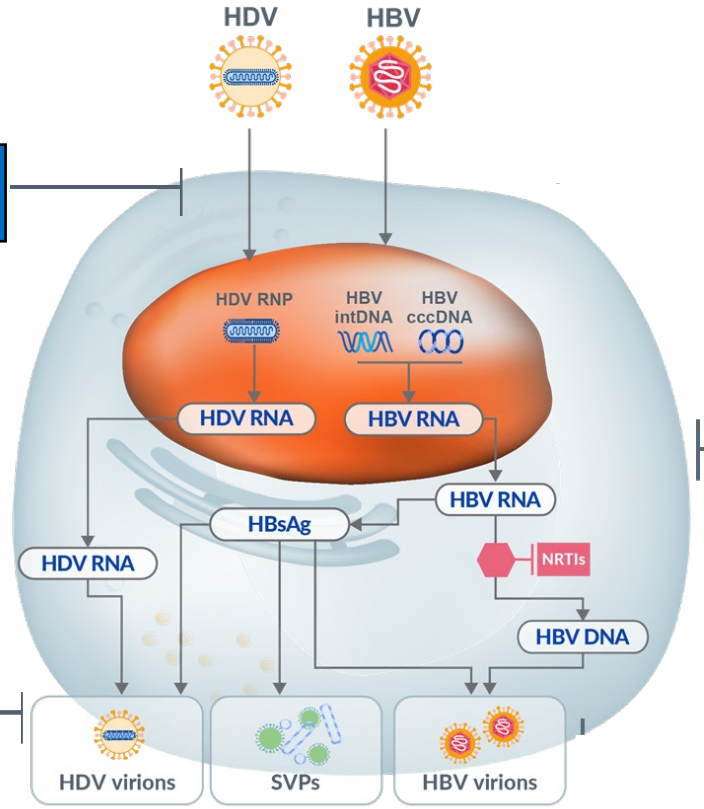
Elebsiran and Tobevibart Mechanisms of Action

Elebsiran reduces HBsAg required for HDV assembly while tobevibart blocks viral entry

Tobevibart[1, 2]

(mAb)

Inhibiting viral entry



Elebsiran[3]

(siRNA)

Degrading HBV RNA and reducing HBsAg production

Neutralizing HDV and HBV virions

Elebsiran, an siRNA, depletes HBsAg which is essential for the hepatitis D lifecycle and complementary to tobevibart, a mAb, that inhibits HBV/HDV entry to hepatocytes

Vir Biotechnology™

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

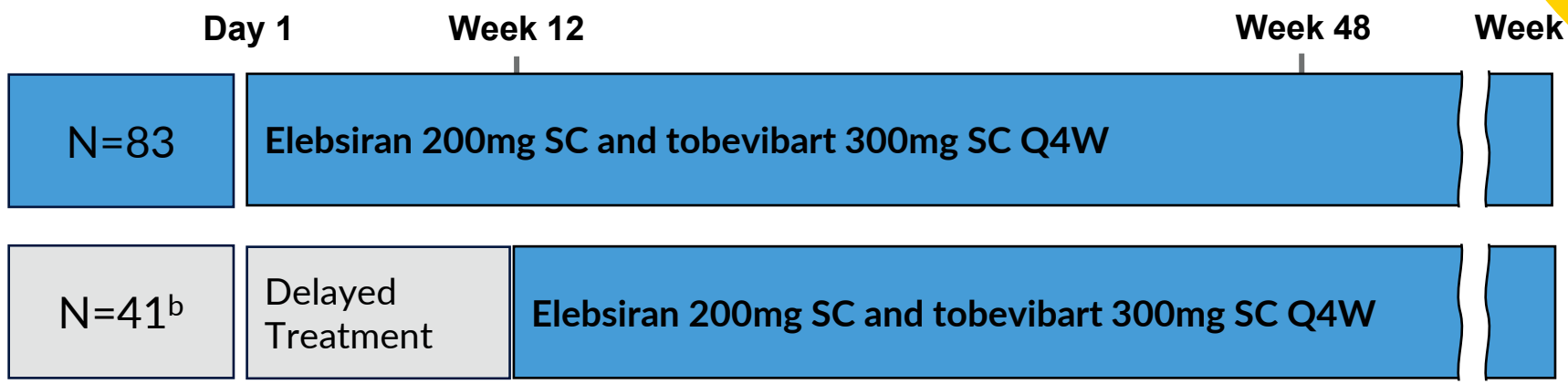
1. Lempp FA, et al. *J Hepatol*. 2023;79(5):1129-1138. 2. Vincenzetti L, et al. *J Hepatol*. 2026; 84(1):62-73. 3. Gane E, et al. *J Hepatol*. 2023;79(4):924-932.

Phase 3 ECLIPSE 1 Study Design

Elebsiran and tobevibart Q4W vs. delayed treatment in participants with chronic HDV infection

HDV RNA >500 IU/mL
ALT >ULN; ALT <5 × ULN
On NRTI
~ 50% Cirrhotic (CTP-A)[a]
Across 10 countries

Randomized 2:1



Predefined:	At Week 48 for Elebsiran and Tobevibart Q4W vs At Week 12 for Delayed Treatment
Primary Endpoint	HDV RNA <LLOQ, TND and ALT ≤ULN
Secondary Endpoints	HDV RNA <LLOQ, TND **(key secondary)**
	HDV RNA <LLOQ
	ALT ≤ULN
	ALT <1.25xULN
	HDV RNA <LLOQ, TND and ALT <1.25xULN

Exploratory Endpoint	HBsAg <10 IU/mL
Safety Endpoint	Incidence of adverse events

ECLIPSE 1 ClinicalTrials.gov Identifier: NCT06903338.
ALT, alanine aminotransferase; CTP, Child-Turcotte-Pugh; EOT, end of treatment; HBsAg, hepatitis B surface antigen; HDV, hepatitis D virus; LLOQ, lower limit of quantification; NRTI, nucleos(t)ide reverse transcriptase inhibitor; Q4W, once every 4 weeks; SC, subcutaneous; TND, target not detected; ULN, upper limit of normal.
[a]Compensated cirrhotic participants: liver biopsy with METAVIR F4, OR liver stiffness ≥15 kPa and ≤25 kPa, OR cirrhotic liver disease based on investigator assessment within 12 months of screening, and a CTP score of 5 or 6, inclusive at screening and at the start of the study.
[b]One participant withdrew from the study during the delayed treatment period, prior to receipt of elebsiran and tobevibart.

Participant Demographics and Baseline Characteristics

	Elebsiran and Tobevibart Q4W N = 83	Delayed Treatment N = 41
Age, y, mean ± SD	43.8 ± 11.6	46.4 ± 10.9
Male, n (%)	55 (66.3)	27 (65.9)
Race, n (%)		
White	41 (49.4)	24 (58.5)
Asian	34 (41.0)	13 (31.7)
Black or African American	7 (8.4)	3 (7.3)
Other	1 (1.2)	1 (2.4)
ALT, U/L, mean ± SD	94.0 ± 42.3	112.6 ± 65.6
HDV RNA, log_{10} IU/mL, mean ± SD	5.4 ± 1.2	5.7 ± 0.9
HDV genotype, gt (%)	gt1 (90.4); gt2 (1.2); gt5 (3.6)	gt1 (87.8); gt5 (7.3)
HBsAg, log_{10} IU/mL, mean ± SD	3.7 ± 0.6	3.7 ± 0.8
HBeAg positive, n (%)	13 (15.7)	10 (24.4)
HBV DNA[a], log_{10} IU/mL, mean ± SD	0.9 ± 0.6	1.0 ± 0.7
Cirrhotic participants[b], n (%)	46 (55.4)	23 (56.1)
CTP Score, n (%)		
5	43 (93.5%)	20 (87.0%)
6	3 (6.5%)	3 (13.0%)
Liver stiffness, kPa, mean ± SD	13.3 ± 5.5	13.7 ± 5.6
Platelets, $x10^9$/L, mean ± SD	167.3 ± 71.8	153.1 ± 54.9
Previously treated with Bulevirtide, n (%)	3 (3.6)	0

ALT, alanine aminotransferase; CTP, Child-Turcotte-Pugh; gt, genotype; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HDV, hepatitis D virus; LLOQ, lower limit of quantification; 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

[a]HBV DNA Categories; <10 IU/mL: 68 (81.9%) in Elebsiran and Tobevibart Q4W, 33 (80.5%) in Delayed Treatment. ≥10 IU/mL: 15 (18.1%) in Elebsiran and Tobevibart Q4W, 8 (19.5%) in Delayed Treatment

[b]Compensated cirrhotic participants: liver biopsy with METAVIR F4, OR liver stiffness ≥15 kPa and ≤25 kPa, OR cirrhotic liver disease based on investigator assessment within 12 months of screening, and a CTP score of 5 or 6, inclusive at screening and at the start of the study.

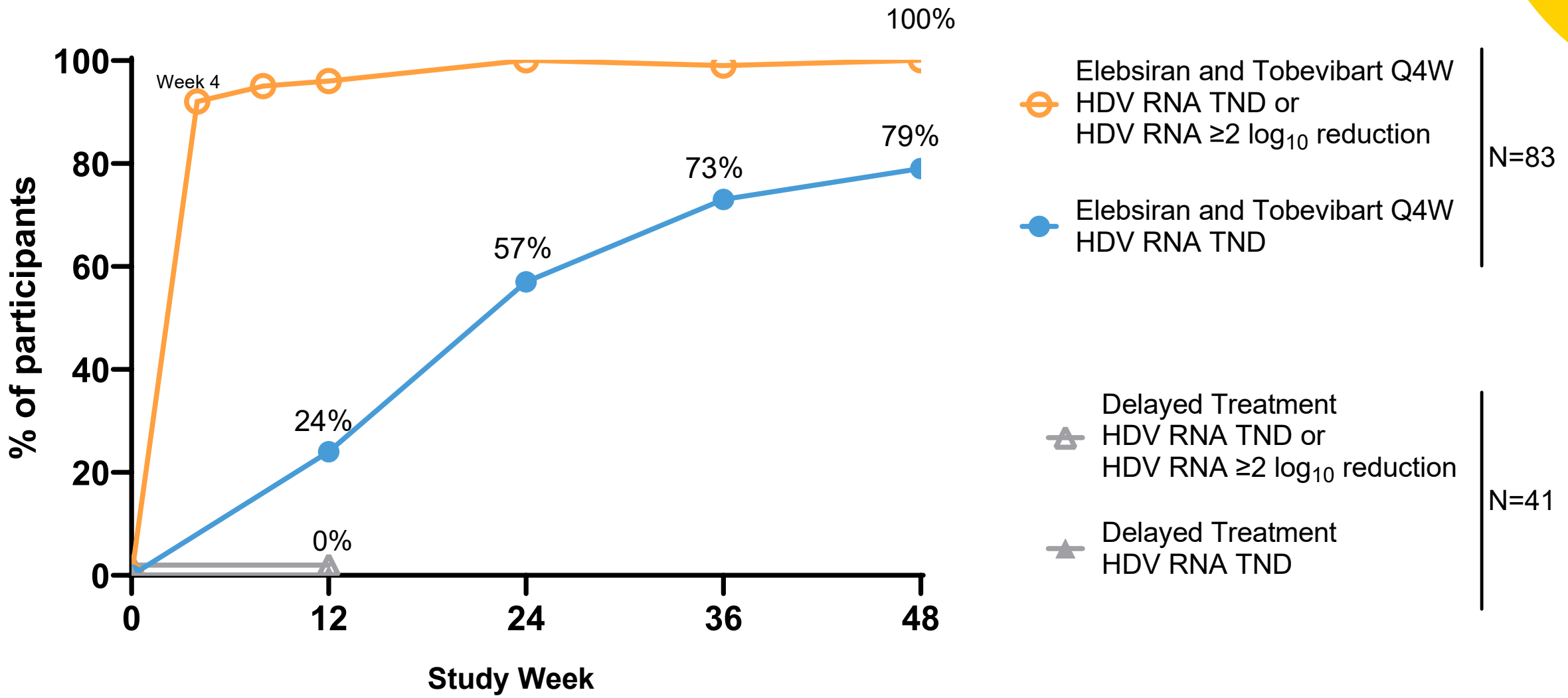
ECLIPSE 1 Primary and Select Secondary and Exploratory Endpoints

The study met its primary and key secondary endpoints

	Elebsiran and Tobevibart Q4W N = 83	Delayed Treatment N = 41	Treatment Difference (95% CI)	P-value
Primary Endpoint Response % HDV RNA <LLOQ TND + ALT ≤ULN	44.1	0.0	44.1 (32.6, 55.0)	<0.0001
Key Secondary Endpoint Response % HDV RNA <LLOQ TND	79.2	0.0	79.2 (69.6, 87.1)	<0.0001
HDV RNA <LLOQ (< 63 IU/mL), n (%)	80 (96.4)	0	96.4 (88.4, 99.4)	<0.0001[a]
HDV RNA < LLOQ TND or HDV RNA ≥2 log_{10} reduction[b], n (%)	83 (100)	0	100.0 (91.4, 100.0)	<0.0001[a]
ALT ≤ULN, n (%)	44 (53.0)	2 (4.9)	48.1 (32.3, 60.3)	<0.0001[a]
ALT <1.25 x ULN, n (%)	57 (68.7)	7 (17.1)	51.6 (32.9, 65.4)	<0.0001[a]
HDV RNA < LLOQ TND + ALT <1.25xULN, n (%)	46 (55.4)	0	55.4 (44.0, 66.3)	<0.0001[a]
HBsAg <10 IU/mL (exploratory), n (%)	79 (95.2)	0	95.2 (87.0, 98.7)	<0.0001[a]

ALT, alanine aminotransferase; CI, confidence interval; HBsAg, hepatitis B surface antigen; HDV, hepatitis D virus; LLOQ, lower limit of quantification; Q4W, once every 4 weeks; TND, target not detected; ULN, upper limit of normal
HDV RNA was measured using RoboGene 2.0 with manual RNA extraction; HDV RNA LLOQ = 63 IU/mL
[a]Nominal p-values
[b]Post hoc analysis

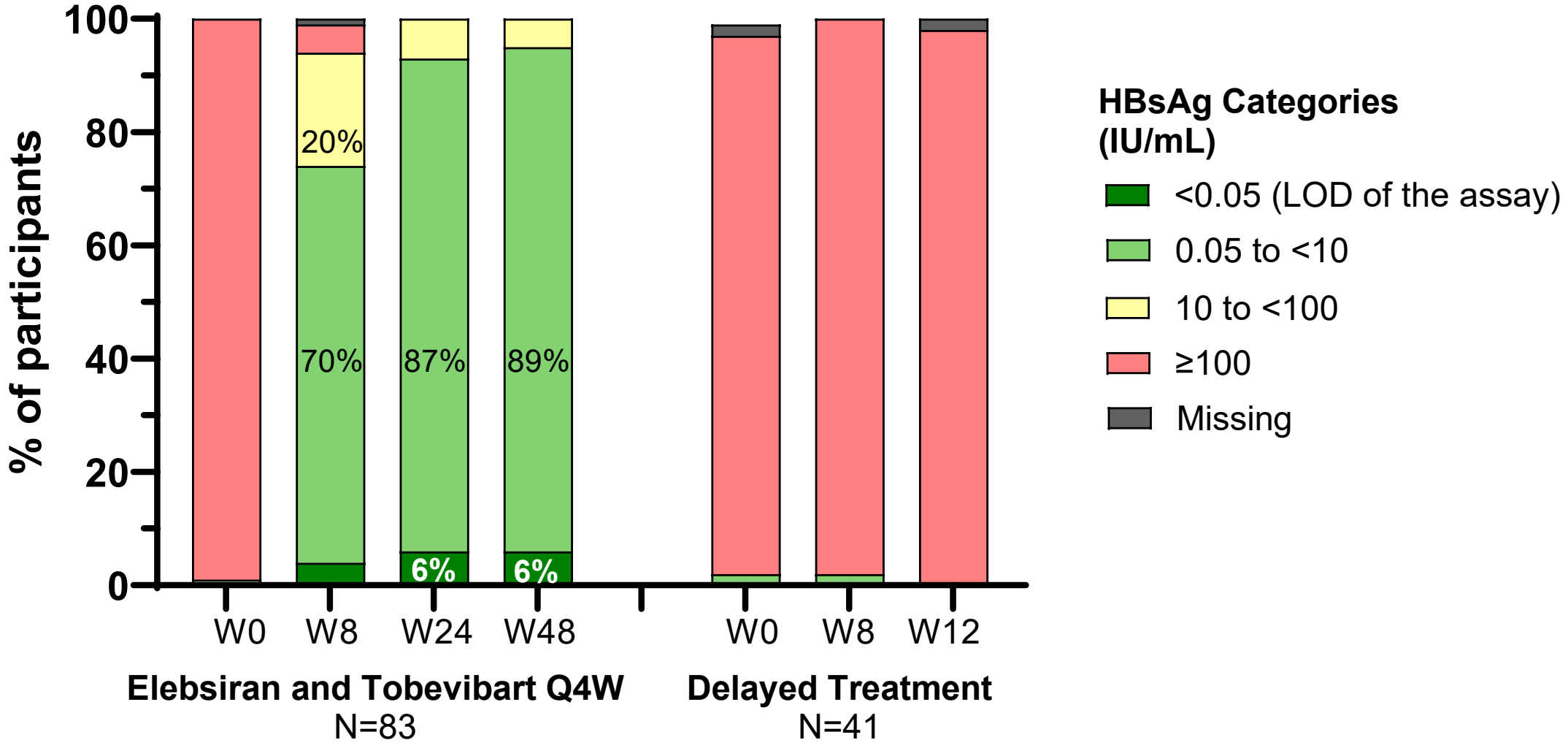
HDV RNA Response Deepens Over Time with Elebsiran and Tobevibart Q4W



HDV, hepatitis D virus; Q4W, once every 4 weeks; TND, target not detected
HDV RNA was measured using RoboGene 2.0 with manual RNA extraction; HDV RNA LLOQ = 63 IU/mL

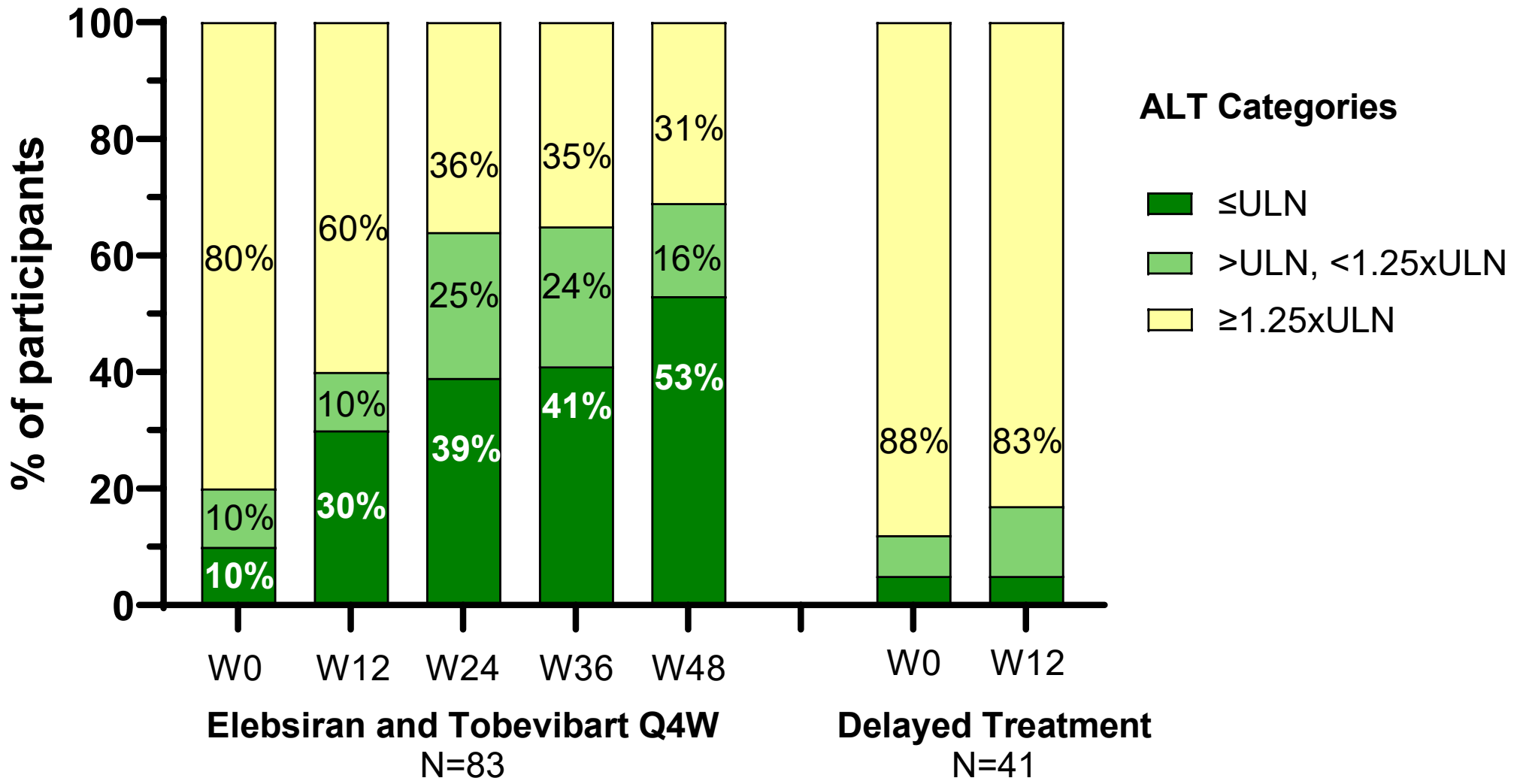
Rapid decline in HBsAg with Elebsiran and Tobevibart Q4W

95% of participants achieved HBsAg <10 IU/mL by Week 48



LOD, limit of detection; Q4W, once every 4 weeks; HBsAg, hepatitis B surface antigen; W, week

ALT Improves Over Time with Elebsiran and Tobevibart Q4W



ALT, alanine aminotransferase; Q4W, once every 4 weeks; ULN, upper limit of normal; W, week
All participants had ALT >ULN at time of screening
ULN of assay: 50 U/L for male; 35 U/L for female

Viral and Biochemical Responses at Week 48 Were Similar in Compensated Cirrhotic and Noncirrhotic Participants

	Elebsiran and Tobevibart Q4W N = 83	
	Noncirrhotic N = 37	**Compensated Cirrhotic[a] N = 46**
HDV RNA <LLOQ, TND + ALT ≤ULN, n (%) [95% CI]	17 (45.9) [29.5, 63.1]	20 (43.5) [28.9, 58.9]
HDV RNA <LLOQ, TND, n (%) [95% CI]	27 (73.0) [55.9, 86.2]	39 (84.8) [71.1, 93.7]
ALT ≤ULN, n (%) [95% CI]	22 (59.5) [42.1, 75.2]	22 (47.8) [32.9, 63.1]

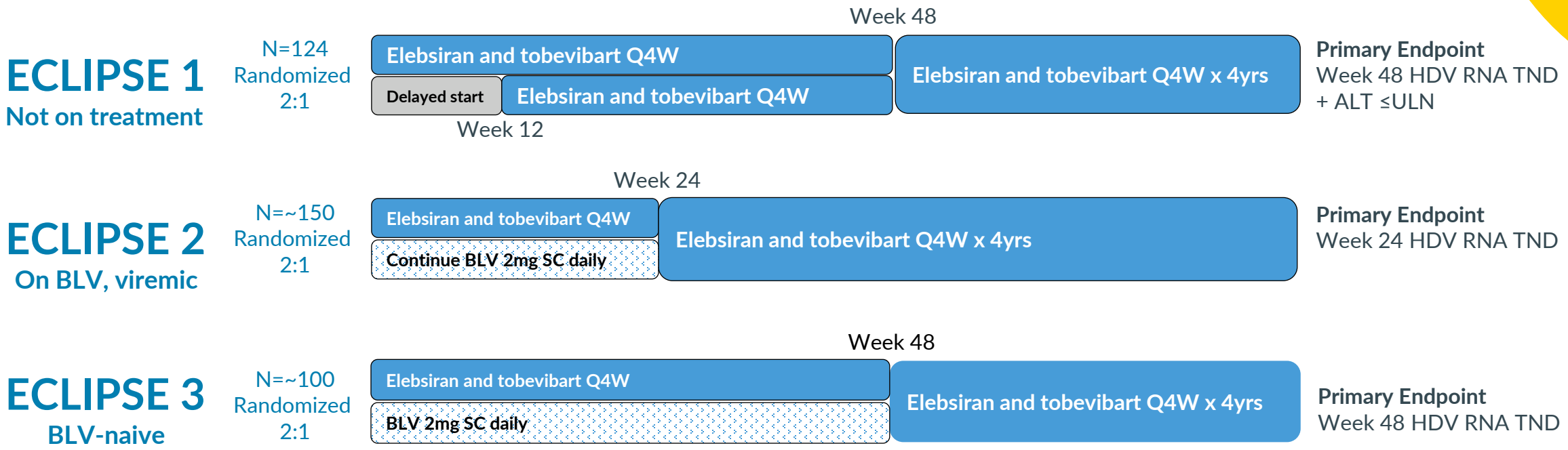
ALT, alanine aminotransferase; HDV, hepatitis D virus; LLOQ, lower limit of quantification; Q4W, once every 4 weeks; TND, target not detected; ULN, upper limit of normal
HDV RNA was measured using RoboGene 2.0 with manual RNA extraction; HDV RNA LLOQ = 63 IU/mL
[a]Compensated cirrhotic participants: liver biopsy with METAVIR F4, OR liver stiffness ≥15 kPa and ≤25 kPa, OR cirrhotic liver disease based on investigator assessment within 12 months of screening, and a CTP score of 5 or 6, inclusive at screening and at the start of the study.

Elebsiran and tobevibart Q4W was well tolerated with all participants completing W48
No participants interrupted or discontinued study drug

Safety or tolerability measure, n (%)[a]	Elebsiran and Tobevibart Q4W[b] N = 83	Delayed Treatment through Week 12 N = 41
Any AE	69 (83.1)[c]	13 (31.7)
Grade 1	22 (26.5)	8 (19.5)
Grade 2	42 (50.6)	3 (7.3)
Grade 3	5 (6.0)[d]	2 (4.9)[e]
Grade 4	0	0
Treatment-related TEAE	59 (71.1)	0
Treatment-emergent flu-like symptoms[f,g] Only 1 episode while on treatment ≥2 episodes while on treatment With first dose	36 (43.4) 30 (36.1) 6 (7.2) 31 (37.3)	NA
Injection site reactions[h]	21 (25.3)	NA
TEAE leading to study drug interruption	0	0
TEAE leading to study drug discontinuation	0	0
Serious AE	0	0

AE, adverse event; Q4W, once every 4 weeks; TEAE, treatment-emergent adverse event.
[a]A participant with multiple events within a category is counted only once in that category.
[b]All available treatment-emergent data up until the data cutoff date of 30Sep2026, inclusive of 48 weeks of elebsiran and tobevibart treatment.
[c]The most frequently reported AEs (≥5% of participants) include influenza-like illness, headache, pyrexia, fatigue, injection site pain, myalgia, chills, injection site erythema, neutrophil count decreased, nausea, upper respiratory tract infection, injection site swelling and nasopharyngitis.
[d]One participant reported neutrophil count decreased (related); one participant reported diabetes mellitus (unrelated); two participants reported dental caries (unrelated); one participant reported skin laceration (unrelated) and hand fracture (unrelated)
[e]One participant reported neutrophil count decreased; one participant reported lymphocyte count decreased and white blood cell decreased
[f]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.
[g]Majority of flu-like symptoms were reported only after the first dose of elebsiran and tobevibart and resolved within 24-48 hours of dosing.
[h]Grouped term that includes multiple preferred terms; 18 (21.7%) were Grade 1; 3 (3.6%) were Grade 2

The ECLIPSE Registrational Program Evaluates Elebsiran and Tobevibart Across Key CHD Populations



ECLIPSE program enrollment completed
Data from ECLIPSE 2 and 3 expected in Q1 2027

CHD, chronic hepatitis delta; BLV, bulevirtide.

Phase 3 ECLIPSE 1 Trial of Q4W Elebsiran and Tobevibart

- ECLIPSE 1 met its primary endpoint at Week 48
  - ***44%** HDV RNA TND plus ALT normalization response vs **0%** in the control*
- ECLIPSE 1 met its key secondary endpoint
  - ***79%** HDV RNA TND response vs **0%** in the control*
- 100% of participants achieved ≥2-$\log_{10}$ reduction of HDV RNA, 53% of participants normalized ALT
- 95% of participants achieved HBsAg <10 IU/mL
- 85% cirrhotic and 73% noncirrhotic participants achieved HDV RNA TND
- Elebsiran and tobevibart is well tolerated with all participants completing 48 weeks of treatment without dose interruption or discontinuation

The combination of siRNA and monoclonal antibody *delivered rapid and profound HDV suppression and HBsAg decline*

Elebsiran and tobevibart have the potential to transform hepatitis D treatment and become the standard of care

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.

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