



Clinical trial results:

A Phase 2a, Open-Label Study to Evaluate the Safety and Efficacy of Selgantolimod (SLGN)-Containing Combination Therapies for the Treatment of Chronic Hepatitis B (CHB)

Summary

EudraCT number	2021-000672-11
Trial protocol	DK
Global end of trial date	19 July 2024

Results information

Result version number	v1 (current)
This version publication date	23 July 2025
First version publication date	23 July 2025

Trial information

Trial identification

Sponsor protocol code	GS-US-465-4439
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04891770
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 July 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 January 2024
Global end of trial reached?	Yes
Global end of trial date	19 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the safety and tolerability of study treatment(s) (selgantolimod-containing combination therapies) and to evaluate the efficacy of study treatment(s) as measured by the proportion of participants who achieved functional cure, defined as hepatitis B surface antigen (HBsAg) loss and hepatitis B virus (HBV) deoxyribonucleic acid (DNA) < lower limit of quantitation (LLOQ) at Follow-up (FU) Week 24 in participants with chronic hepatitis B (CHB).

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements. This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 August 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	11 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Hong Kong: 36
Country: Number of subjects enrolled	New Zealand: 5
Country: Number of subjects enrolled	Singapore: 14
Country: Number of subjects enrolled	Korea, Republic of: 9
Country: Number of subjects enrolled	Thailand: 26
Country: Number of subjects enrolled	United Kingdom: 5
Worldwide total number of subjects	103
EEA total number of subjects	3

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	103
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Australia, Denmark, Hong Kong, New Zealand, Singapore, South Korea, Thailand, and the United Kingdom.

Pre-assignment

Screening details:

165 participants were screened.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

In the viremic cohorts, participants were randomized 2:1 into Cohort 2 Groups A and B.

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: TAF + VIR-2218 + SLGN + Nivolumab

Arm description:

Nucleos(t)ide(s) (NUC)-suppressed participants with chronic hepatitis B (CHB) received tenofovir alafenamide (TAF) 25 mg orally once daily (QD) for 36 weeks and VIR-2218 200 mg subcutaneously (SC) once every 4 weeks (Q4W) for 24 weeks. From Week 12 onwards, participants also received selgantolimod (SLGN) 3 mg orally once a week (QW) for 24 weeks and nivolumab 0.3 mg/kg intravenously (IV) Q4W for up to 24 weeks (only up to protocol amendment 2, nivolumab was no longer administered post implementation of protocol amendment 2). Participants who were on TAF treatment continued TAF treatment over the duration of study follow-up. Participants were followed up for 48 weeks post treatment.

Arm type	Experimental
Investigational medicinal product name	Tenofovir Alafenamide
Investigational medicinal product code	
Other name	TAF, GS-7340, Vemlidy®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg administered once daily for 36 weeks

Investigational medicinal product name	Selgantolimod
Investigational medicinal product code	
Other name	SLGN, GS-9688
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

3 mg administered once a week for 24 weeks

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	Opdivo®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.3 mg/kg administered once every 4 weeks for up to 24 weeks

Investigational medicinal product name	VIR-2218
Investigational medicinal product code	
Other name	ALN-HBV-02, ALN-81890, AD-81890
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
200 mg administered once every 4 weeks for 24 weeks	
Arm title	Cohort 2 Group A: VIR-2218 + SLGN + Nivolumab

Arm description:

Viremic participants with CHB received VIR-2218, 200 mg SC Q4W for 24 weeks. From Week 12 onwards, participants also received SLGN 3 mg orally QW for 24 weeks and nivolumab 0.3 mg/kg IV Q4W for up to 24 weeks (only up to protocol amendment 2, nivolumab was no longer administered post implementation of protocol amendment 2). Participants who met the criteria to initiate NUC treatment received TAF 25 mg orally, QD during the study. Participants were followed up for 48 weeks post treatment.

Arm type	Experimental
Investigational medicinal product name	VIR-2218
Investigational medicinal product code	
Other name	ALN-HBV-02, ALN-81890, AD-81890
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

200 mg administered once every 4 weeks for 24 weeks

Investigational medicinal product name	Selgantolimod
Investigational medicinal product code	
Other name	SLGN, GS-9688
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

3 mg administered once a week for 24 weeks

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	Opdivo®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.3 mg/kg administered once every 4 weeks for up to 24 weeks

Arm title	Cohort 2 Group B: SLGN + Nivolumab
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Arm description:

Viremic participants with CHB received SLGN 3 mg orally QW for 24 weeks and nivolumab 0.3 mg/kg IV Q4W for up to 24 weeks.

Viremic participants who met the criteria to initiate NUC treatment received TAF 25 mg orally QD during the study. Participants were followed up for 48 weeks post treatment.

All treatments were administered up to protocol amendment 2 and after the implementation of protocol amendment 2, the treatments were discontinued for Cohort 2 Group B based on Sponsor decision.

Arm type	Experimental
Investigational medicinal product name	Selgantolimod
Investigational medicinal product code	
Other name	SLGN, GS-9688
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

3 mg administered once a week for 24 weeks

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	Opdivo®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.3 mg/kg administered once every 4 weeks for up to 24 weeks

Number of subjects in period 1^[1]	Cohort 1: TAF + VIR-2218 + SLGN + Nivolumab	Cohort 2 Group A: VIR-2218 + SLGN + Nivolumab	Cohort 2 Group B: SLGN + Nivolumab
Started	42	40	20
Completed	41	36	20
Not completed	1	4	0
Withdrew consent	1	3	-
Investigator's discretion	-	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: One participant was enrolled but did not receive study drug in Cohort 2 Group B: SLGN + Nivolumab.

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: TAF + VIR-2218 + SLGN + Nivolumab
Reporting group description:	
Nucleos(t)ide(s) (NUC)-suppressed participants with chronic hepatitis B (CHB) received tenofovir alafenamide (TAF) 25 mg orally once daily (QD) for 36 weeks and VIR-2218 200 mg subcutaneously (SC) once every 4 weeks (Q4W) for 24 weeks. From Week 12 onwards, participants also received selgantolimod (SLGN) 3 mg orally once a week (QW) for 24 weeks and nivolumab 0.3 mg/kg intravenously (IV) Q4W for up to 24 weeks (only up to protocol amendment 2, nivolumab was no longer administered post implementation of protocol amendment 2). Participants who were on TAF treatment continued TAF treatment over the duration of study follow-up. Participants were followed up for 48 weeks post treatment.	
Reporting group title	Cohort 2 Group A: VIR-2218 + SLGN + Nivolumab
Reporting group description:	
Viremic participants with CHB received VIR-2218, 200 mg SC Q4W for 24 weeks. From Week 12 onwards, participants also received SLGN 3 mg orally QW for 24 weeks and nivolumab 0.3 mg/kg IV Q4W for up to 24 weeks (only up to protocol amendment 2, nivolumab was no longer administered post implementation of protocol amendment 2). Participants who met the criteria to initiate NUC treatment received TAF 25 mg orally, QD during the study. Participants were followed up for 48 weeks post treatment.	
Reporting group title	Cohort 2 Group B: SLGN + Nivolumab
Reporting group description:	
Viremic participants with CHB received SLGN 3 mg orally QW for 24 weeks and nivolumab 0.3 mg/kg IV Q4W for up to 24 weeks.	
Viremic participants who met the criteria to initiate NUC treatment received TAF 25 mg orally QD during the study. Participants were followed up for 48 weeks post treatment.	
All treatments were administered up to protocol amendment 2 and after the implementation of protocol amendment 2, the treatments were discontinued for Cohort 2 Group B based on Sponsor decision.	

Reporting group values	Cohort 1: TAF + VIR-2218 + SLGN + Nivolumab	Cohort 2 Group A: VIR-2218 + SLGN + Nivolumab	Cohort 2 Group B: SLGN + Nivolumab
Number of subjects	42	40	20
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	48	42	44
standard deviation	± 8.1	± 7.9	± 7.9
Gender categorical			
Units: Subjects			
Female	16	25	10
Male	26	15	10
Race			
Units: Subjects			
Asian	41	37	18
Black or African American	1	2	0
Other or More Than One Race	0	1	2
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	40	39	20

Not Collected	2	1	0
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Reporting group values	Total		
Number of subjects	102		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	51		
Male	51		
Race Units: Subjects			
Asian	96		
Black or African American	3		
Other or More Than One Race	3		
Ethnicity Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	99		
Not Collected	3		

End points

End points reporting groups

Reporting group title	Cohort 1: TAF + VIR-2218 + SLGN + Nivolumab
Reporting group description: Nucleos(t)ide(s) (NUC)-suppressed participants with chronic hepatitis B (CHB) received tenofovir alafenamide (TAF) 25 mg orally once daily (QD) for 36 weeks and VIR-2218 200 mg subcutaneously (SC) once every 4 weeks (Q4W) for 24 weeks. From Week 12 onwards, participants also received selgantolimod (SLGN) 3 mg orally once a week (QW) for 24 weeks and nivolumab 0.3 mg/kg intravenously (IV) Q4W for up to 24 weeks (only up to protocol amendment 2, nivolumab was no longer administered post implementation of protocol amendment 2). Participants who were on TAF treatment continued TAF treatment over the duration of study follow-up. Participants were followed up for 48 weeks post treatment.	
Reporting group title	Cohort 2 Group A: VIR-2218 + SLGN + Nivolumab
Reporting group description: Viremic participants with CHB received VIR-2218, 200 mg SC Q4W for 24 weeks. From Week 12 onwards, participants also received SLGN 3 mg orally QW for 24 weeks and nivolumab 0.3 mg/kg IV Q4W for up to 24 weeks (only up to protocol amendment 2, nivolumab was no longer administered post implementation of protocol amendment 2). Participants who met the criteria to initiate NUC treatment received TAF 25 mg orally, QD during the study. Participants were followed up for 48 weeks post treatment.	
Reporting group title	Cohort 2 Group B: SLGN + Nivolumab
Reporting group description: Viremic participants with CHB received SLGN 3 mg orally QW for 24 weeks and nivolumab 0.3 mg/kg IV Q4W for up to 24 weeks. Viremic participants who met the criteria to initiate NUC treatment received TAF 25 mg orally QD during the study. Participants were followed up for 48 weeks post treatment. All treatments were administered up to protocol amendment 2 and after the implementation of protocol amendment 2, the treatments were discontinued for Cohort 2 Group B based on Sponsor decision.	

Primary: Percentage of Participants Who Achieve Functional Cure

End point title	Percentage of Participants Who Achieve Functional Cure
End point description: Functional cure was defined as hepatitis B surface antigen (HBsAg) loss and hepatitis B virus (HBV) deoxyribonucleic acid (DNA) less than the lower limit of quantitation (LLOQ) at follow-up Week 24. LLOQ for HBV DNA CAP/CTM 2.0 is 20 IU/mL. LLOQ for HBV DNA Cobas 6800 is 10 IU/mL. The HBsAg loss was defined as HBsAg changing from positive at baseline to negative at any postbaseline visit. Percentages were rounded-off. The Full Analysis Set included all enrolled participants in Cohort 1, or all randomized participants in Cohort 2 who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe: At Follow-up Week 24 (Cohort 1 and Cohort 2A: At Week 60; Cohort 2B: At Week 48)	

End point values	Cohort 1: TAF + VIR-2218 + SLGN + Nivolumab	Cohort 2 Group A: VIR-2218 + SLGN + Nivolumab	Cohort 2 Group B: SLGN + Nivolumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	40	20	
Units: percentage of participants				
number (confidence interval 95%)	2.4 (0.1 to 12.6)	2.5 (0.1 to 13.2)	0.0 (0.0 to 16.8)	

Statistical analyses

Statistical analysis title	Cohort 2 Group A vs Cohort 2 Group B
Statistical analysis description: For Cohort 2A versus Cohort 2B, the percentage difference and the corresponding 95% confidence interval was calculated using the stratum-adjusted Mantel-Haenszel method, stratified by HBsAg group (> 3 and ≤ 3 log ₁₀ IU/mL).	
Comparison groups	Cohort 2 Group A: VIR-2218 + SLGN + Nivolumab v Cohort 2 Group B: SLGN + Nivolumab
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	percentage difference
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	7.3

Secondary: Percentage of Participants With Hepatitis B Surface Antigen (HBsAg) Loss With and Without Anti-HBsAg Seroconversion

End point title	Percentage of Participants With Hepatitis B Surface Antigen (HBsAg) Loss With and Without Anti-HBsAg Seroconversion
End point description: HBsAg loss was defined as HBsAg changing from positive at baseline to negative at any postbaseline visit. HBsAg seroconversion was defined as HBsAg loss and HBsAb changes from negative/missing at baseline to positive at a postbaseline visit. Percentages were rounded-off. Participants in the Full Analysis Set were analyzed. 9999= In Cohort 2 Group B, participants received study treatment for up to 24 weeks. Thereafter, participants were followed up for 48 weeks. Therefore, data for Weeks 28, 32, and 36 are not reported for this cohort in this outcome measure.	
End point type	Secondary
End point timeframe: Up to Follow-up Week 48 (Cohort 1 and Cohort 2A: At Week 84; Cohort 2B: At Week 72)	

End point values	Cohort 1: TAF + VIR-2218 + SLGN + Nivolumab	Cohort 2 Group A: VIR-2218 + SLGN + Nivolumab	Cohort 2 Group B: SLGN + Nivolumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	40	20	
Units: percentage of participants				
number (not applicable)				

HBsAg Loss: Week (WK) 4 (n=42,40,20)	0	0	0	
HBsAg Loss and Seroconversion: Wk 4 (n=42,40,20)	0	0	0	
HBsAg Loss: WK 8 (n=42,40,20)	0	0	0	
HBsAg Loss and Seroconversion: Wk 8 (n=42,40,20)	0	0	0	
HBsAg Loss: Wk 12 (n=42,40,20)	2.4	0	0	
HBsAg Loss and Seroconversion: Wk 12 (n=42,40,20)	0	0	0	
HBsAg Loss: Wk 14 (n=42,40,20)	2.4	0	0	
HBsAg Loss and Seroconversion: Wk 14 (n=42,40,20)	0	0	0	
HBsAg Loss: Wk 16 (n=42,40,20)	0	0	0	
HBsAg Loss and Seroconversion: Wk 16 (n=42,40,20)	0	0	0	
HBsAg Loss: Wk 20 (n=42,40,20)	4.8	2.5	0	
HBsAg Loss and Seroconversion: Wk 20 (n=42,40,20)	0	0	0	
HBsAg Loss: Wk 24 (n=42,40,20)	4.8	0	0	
HBsAg Loss and Seroconversion: Wk 24 (n=42,40,20)	0	0	0	
HBsAg Loss: Wk 28 (n=42,40,0)	4.8	0	9999	
HBsAg Loss and Seroconversion: Wk 28 (n=42,40,0)	0	0	9999	
HBsAg Loss: Wk 32 (n=42,40,0)	4.8	0	9999	
HBsAg Loss and Seroconversion: Wk 32 (n=42,40,0)	0	0	9999	
HBsAg Loss: Wk 36 (n=42,40,0)	4.8	0	9999	
HBsAg Loss and Seroconversion: Wk 36 (n=42,40,0)	0	0	9999	
HBsAg Loss: Follow-up (FU) Wk 2 (n=42,40,20)	4.8	0	0	
HBsAg Loss and Seroconversion: FU Wk 2 (n=42,40,20)	0	0	0	
HBsAg Loss: FU Wk 4 (n=42,40,20)	4.8	0	0	
HBsAg Loss and Seroconversion: FU Wk 4 (n=42,40,20)	0	0	0	
HBsAg Loss: FU Wk 8 (n=42,40,20)	4.8	0	0	
HBsAg Loss and Seroconversion: FU Wk 8 (n=42,40,20)	0	0	0	
HBsAg Loss: FU Wk 12 (n=42,40,20)	7.1	0	0	
HBsAg Loss and Seroconversion: FU Wk 12(n=42,40,20)	0	0	0	
HBsAg Loss: FU Wk 24 (n=42,40,20)	4.8	2.5	0	
HBsAg Loss and Seroconversion: FU Wk 24(n=42,40,20)	0	0	0	
HBsAg Loss: FU Wk 36 (n=42,40,20)	7.1	2.5	0	
HBsAg Loss and Seroconversion: FU Wk 36(n=42,40,20)	2.4	0	0	
HBsAg Loss: FU Wk 48 (n=42,40,20)	7.1	2.5	0	
HBsAg Loss and Seroconversion: FU Wk 48(n=42,40,20)	0	0	0	

Statistical analyses

Secondary: Percentage of Participants With Hepatitis B e Antigen (HBeAg) Loss With and Without Anti-HBeAg Seroconversion in Participants With CHB Who Are HBeAg-Positive at Baseline

End point title	Percentage of Participants With Hepatitis B e Antigen (HBeAg) Loss With and Without Anti-HBeAg Seroconversion in Participants With CHB Who Are HBeAg-Positive at Baseline
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End point description:

HBeAg loss is defined as HBeAg changing from positive at baseline to negative at any postbaseline visit. HBeAg seroconversion was defined as HBeAb test changing from negative or missing at baseline to positive at a postbaseline visit. Percentages were rounded-off. Participants in the Full Analysis Set with HBeAg positive at Baseline were analyzed. 9999= In Cohort 2 Group B, participants received study treatment for up to 24 weeks. Thereafter, participants were followed up for 48 weeks. Therefore, data for Weeks 28, 32, and 36 are not available for this cohort in this outcome measure.

End point type	Secondary
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End point timeframe:

Up to Follow-up Week 48 (Cohort 1 and Cohort 2A: At Week 84; Cohort 2B: At Week 72)

End point values	Cohort 1: TAF + VIR-2218 + SLGN + Nivolumab	Cohort 2 Group A: VIR-2218 + SLGN + Nivolumab	Cohort 2 Group B: SLGN + Nivolumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	16	6	
Units: percentage of participants				
number (not applicable)				
HBeAg Loss: Wk 4 (n=18,16,6)	5.6	0	0	
HBeAg Loss and Seroconversion: Wk 4 (n=18,16,6)	0	0	0	
HBeAg Loss: Wk 8 (n=18,16,6)	11.1	6.3	0	
HBeAg Loss and Seroconversion: Wk 8 (n=18,16,6)	0	0	0	
HBeAg Loss: Wk 12 (n=18,16,6)	11.1	6.3	0	
HBeAg Loss and Seroconversion: Wk 12 (n=18,16,6)	0	0	0	
HBeAg Loss: Wk 14 (n=18,16,6)	11.1	6.3	0	
HBeAg Loss and Seroconversion: Wk 14 (n=18,16,6)	0	0	0	
HBeAg Loss: Wk 16 (n=18,16,6)	11.1	6.3	0	
HBeAg Loss and Seroconversion: Wk 16 (n=18,16,6)	0	0	0	
HBeAg Loss: Wk 20 (n=18,16,6)	11.1	6.3	0	
HBeAg Loss and Seroconversion: Wk 20 (n=18,16,6)	0	0	0	
HBeAg Loss: Wk 24 (n=18,16,6)	16.7	6.3	0	
HBeAg Loss and Seroconversion: Wk 24 (n=18,16,6)	5.6	0	0	
HBeAg Loss: Wk 28 (n=18,16,0)	16.7	6.3	9999	
HBeAg Loss and Seroconversion: Wk 28 (n=18,16,0)	5.6	0	9999	
HBeAg Loss: Wk 32 (n=18,16,0)	11.1	0	9999	
HBeAg Loss and Seroconversion: Wk 32 (n=18,16,0)	5.6	0	9999	
HBeAg Loss: Wk 36 (n=18,16,0)	11.1	0	9999	

HBeAg Loss and Seroconversion: Wk 36 (n=18,16,0)	5.6	0	9999	
HBeAg Loss: FU Wk 2 (n=18,16,6)	5.6	6.3	0	
HBeAg Loss and Seroconversion: FU Wk 2(n=18,16,6)	0	6.3	0	
HBeAg Loss: FU Wk 4 (n=18,16,6)	16.7	6.3	0	
HBeAg Loss and Seroconversion: FU Wk 4(n=18,16,6)	5.6	6.3	0	
HBeAg Loss: FU Wk 8 (n=18,16,6)	11.1	6.3	0	
HBeAg Loss and Seroconversion: FU Wk 8(n=18,16,6)	0	6.3	0	
HBeAg Loss: FU Wk 12 (n=18,16,6)	16.7	6.3	0	
HBeAg Loss and Seroconversion: FU Wk 12(n=18,16,6)	5.6	6.3	0	
HBeAg Loss: FU Wk 24 (n=18,16,6)	5.6	12.5	0	
HBeAg Loss and Seroconversion: FU Wk 24(n=18,16,6)	0	12.5	0	
HBeAg Loss: FU Wk 36 (n=18,16,6)	11.1	12.5	0	
HBeAg Loss and Seroconversion: FU Wk 36(n=18,16,6)	0	6.3	0	
HBeAg Loss: FU Wk 48 (n=18,16,6)	16.7	12.5	0	
HBeAg Loss and Seroconversion: FU Wk 48(n=18,16,6)	5.6	6.3	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Remain Off NUC Treatment During Follow-Up

End point title	Percentage of Participants Who Remain Off NUC Treatment During Follow-Up
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End point description:

NUC treatments included for analysis: adefovir dipivoxil, entecavir, telbivudine, tenofovir, tenofovir alafenamide, tenofovir alafenamide fumarate, tenofovir disoproxil fumarate, and lamivudine. Percentages were rounded-off. The Follow-Up Analysis Set included all participants who have at least 1 follow-up visit, after completing or premature discontinued from the study drugs.

End point type	Secondary
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End point timeframe:

Cohort 1 and Cohort 2A: From Week 36 up to Week 84 and for Cohort 2B: From Week 24 up to Week 72

End point values	Cohort 1: TAF + VIR-2218 + SLGN + Nivolumab	Cohort 2 Group A: VIR-2218 + SLGN + Nivolumab	Cohort 2 Group B: SLGN + Nivolumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	36	20	
Units: percentage of participants				
number (not applicable)	16.7	55.6	75.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Hepatitis B Virus (HBV) Virologic Breakthrough During Study Treatments

End point title	Percentage of Participants Experiencing Hepatitis B Virus (HBV) Virologic Breakthrough During Study Treatments
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End point description:

Virologic breakthrough was defined as confirmed HBV DNA \geq LLOQ after 2 consecutive HBV DNA $<$ LLOQ in participants who are complying with NUC therapy or confirmed HBV DNA $\geq 1 \log_{10}$ IU/mL increase from nadir during study treatments. LLOQ for HBV DNA CAP/CTM 2.0 is 20 IU/mL. LLOQ for HBV DNA Cobas 6800 is 10 IU/mL. Percentages were rounded-off. Participants in the Full Analysis Set were analyzed.

End point type	Secondary
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End point timeframe:

Up to 36 Weeks

End point values	Cohort 1: TAF + VIR-2218 + SLGN + Nivolumab	Cohort 2 Group A: VIR-2218 + SLGN + Nivolumab	Cohort 2 Group B: SLGN + Nivolumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	40	20	
Units: percentage of participants				
number (not applicable)	7.1	35.0	20.0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause Mortality: Up to 86.4 weeks; Adverse events: Up to 84 weeks

Adverse event reporting additional description:

All-cause Mortality: The All Enrolled Analysis Set included all participants in Cohort 1 who received a study participant identification number in the study after screening, or all participants in Cohort 2 who were randomized in the study. Adverse events: The Safety Analysis Set includes all participants who received at least 1 dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.1
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Reporting groups

Reporting group title	Cohort 1: TAF + VIR-2218 + SLGN + Nivolumab
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Reporting group description:

NUC -suppressed participants with CHB received TAF 25 mg orally QD for 36 weeks and VIR-2218 200 mg SC Q4W for 24 weeks. From Week 12 onwards, participants also received SLGN 3 mg orally QW for 24 weeks and nivolumab 0.3 mg/kg IV Q4W for up to 24 weeks (only up to protocol amendment 2, nivolumab was no longer administered post implementation of protocol amendment 2). Participants who were on TAF treatment continued TAF treatment over the duration of study follow-up for 48 weeks. Participants were followed up for 48 weeks post treatment.

Reporting group title	Cohort 2 Group B: SLGN + Nivolumab
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Reporting group description:

Viremic participants with CHB received SLGN 3 mg orally QW for 24 weeks and nivolumab 0.3 mg/kg IV Q4W for up to 24 weeks. Viremic participants who met the criteria to initiate NUC treatment received TAF 25 mg orally QD for up to 36 weeks during the study. Participants were followed up for 48 weeks post treatment. All treatments were administered up to protocol amendment 2 and after the implementation of protocol amendment 2, the treatments were discontinued for Cohort 2 Group B based on Sponsor decision.

Reporting group title	Cohort 2 Group A: VIR-2218 + SLGN + Nivolumab
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Reporting group description:

Viremic participants with CHB received SLGN 3 mg orally QW for 24 weeks and nivolumab 0.3 mg/kg IV Q4W for up to 24 weeks. Viremic participants who met the criteria to initiate NUC treatment received TAF 25 mg orally QD for up to 36 weeks during the study. Participants were followed up for 48 weeks post treatment. All treatments were administered up to protocol amendment 2 and after the implementation of protocol amendment 2, the treatments were discontinued for Cohort 2 Group B based on Sponsor decision.

Serious adverse events	Cohort 1: TAF + VIR-2218 + SLGN + Nivolumab	Cohort 2 Group B: SLGN + Nivolumab	Cohort 2 Group A: VIR-2218 + SLGN + Nivolumab
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 42 (4.76%)	3 / 20 (15.00%)	5 / 40 (12.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Upper limb fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Immune-mediated hepatitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Chronic hepatitis B			
subjects affected / exposed	0 / 42 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19			
subjects affected / exposed	1 / 42 (2.38%)	0 / 20 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	1 / 42 (2.38%)	0 / 20 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Cohort 1: TAF + VIR-2218 + SLGN + Nivolumab	Cohort 2 Group B: SLGN + Nivolumab	Cohort 2 Group A: VIR-2218 + SLGN + Nivolumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 42 (80.95%)	19 / 20 (95.00%)	37 / 40 (92.50%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 42 (7.14%)	0 / 20 (0.00%)	0 / 40 (0.00%)
occurrences (all)	3	0	0
Surgical and medical procedures			
Wisdom teeth removal			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	7 / 42 (16.67%)	2 / 20 (10.00%)	4 / 40 (10.00%)
occurrences (all)	8	9	12
Fatigue			
subjects affected / exposed	4 / 42 (9.52%)	4 / 20 (20.00%)	7 / 40 (17.50%)
occurrences (all)	4	5	14
Pyrexia			
subjects affected / exposed	4 / 42 (9.52%)	0 / 20 (0.00%)	5 / 40 (12.50%)
occurrences (all)	4	0	8
Injection site pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 20 (0.00%)	6 / 40 (15.00%)
occurrences (all)	0	0	11

Malaise subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	2 / 20 (10.00%) 2	1 / 40 (2.50%) 2
Injection site reaction subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	0 / 20 (0.00%) 0	2 / 40 (5.00%) 2
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	0 / 20 (0.00%) 0	2 / 40 (5.00%) 2
Reproductive system and breast disorders Menstruation irregular subjects affected / exposed occurrences (all) Heavy menstrual bleeding subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0 0 / 42 (0.00%) 0	2 / 20 (10.00%) 2 1 / 20 (5.00%) 1	1 / 40 (2.50%) 1 0 / 40 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Rhinitis allergic subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	2 / 42 (4.76%) 2 0 / 42 (0.00%) 0 0 / 42 (0.00%) 0	0 / 20 (0.00%) 0 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1	2 / 40 (5.00%) 3 1 / 40 (2.50%) 1 0 / 40 (0.00%) 0
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1	0 / 20 (0.00%) 0	2 / 40 (5.00%) 2
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased	2 / 42 (4.76%) 3	4 / 20 (20.00%) 4	11 / 40 (27.50%) 11

subjects affected / exposed	2 / 42 (4.76%)	1 / 20 (5.00%)	4 / 40 (10.00%)
occurrences (all)	2	1	4
Alanine aminotransferase abnormal			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Eye injury			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Synovial rupture			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 42 (2.38%)	0 / 20 (0.00%)	2 / 40 (5.00%)
occurrences (all)	1	0	2
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 42 (14.29%)	4 / 20 (20.00%)	6 / 40 (15.00%)
occurrences (all)	7	12	8
Dizziness			
subjects affected / exposed	4 / 42 (9.52%)	2 / 20 (10.00%)	6 / 40 (15.00%)
occurrences (all)	6	3	6
Dysgeusia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 20 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	3
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	1 / 40 (2.50%)
occurrences (all)	0	1	1
Vision blurred			

subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	1 / 40 (2.50%)
occurrences (all)	0	1	1
Dry eye			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Eye pain			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Ocular discomfort			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Optic neuropathy			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Pseudopapilloedema			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	16 / 42 (38.10%)	10 / 20 (50.00%)	27 / 40 (67.50%)
occurrences (all)	62	54	99
Vomiting			
subjects affected / exposed	8 / 42 (19.05%)	9 / 20 (45.00%)	15 / 40 (37.50%)
occurrences (all)	29	28	29
Diarrhoea			
subjects affected / exposed	3 / 42 (7.14%)	3 / 20 (15.00%)	7 / 40 (17.50%)
occurrences (all)	3	5	8
Abdominal discomfort			
subjects affected / exposed	1 / 42 (2.38%)	1 / 20 (5.00%)	2 / 40 (5.00%)
occurrences (all)	1	1	2
Dyspepsia			
subjects affected / exposed	3 / 42 (7.14%)	0 / 20 (0.00%)	0 / 40 (0.00%)
occurrences (all)	3	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0

Lip ulceration subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	1 / 20 (5.00%) 1	0 / 40 (0.00%) 0
Hepatobiliary disorders Hypertransaminasaemia subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	2 / 20 (10.00%) 2	3 / 40 (7.50%) 3
Skin and subcutaneous tissue disorders Skin lesion subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	1 / 20 (5.00%) 1	0 / 40 (0.00%) 0
Psoriasis subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	1 / 20 (5.00%) 1	0 / 40 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1	1 / 20 (5.00%) 1	1 / 40 (2.50%) 1
Rash pruritic subjects affected / exposed occurrences (all)	3 / 42 (7.14%) 3	0 / 20 (0.00%) 0	0 / 40 (0.00%) 0
Acne subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	0 / 20 (0.00%) 0	2 / 40 (5.00%) 2
Dermatitis subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	0 / 20 (0.00%) 0	2 / 40 (5.00%) 2
Erythema subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	0 / 20 (0.00%) 0	2 / 40 (5.00%) 2
Alopecia subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	1 / 20 (5.00%) 1	0 / 40 (0.00%) 0
Urticaria subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	1 / 20 (5.00%) 1	0 / 40 (0.00%) 0
Renal and urinary disorders			

Dysuria subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1	1 / 20 (5.00%) 1	0 / 40 (0.00%) 0
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	3 / 42 (7.14%) 5	1 / 20 (5.00%) 1	1 / 40 (2.50%) 1
Infections and infestations Covid-19 subjects affected / exposed occurrences (all)	16 / 42 (38.10%) 17	4 / 20 (20.00%) 4	10 / 40 (25.00%) 10
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 2	2 / 20 (10.00%) 2	1 / 40 (2.50%) 1
Anal abscess subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1	1 / 20 (5.00%) 1	0 / 40 (0.00%) 0
Hepatitis B subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	0 / 20 (0.00%) 0	2 / 40 (5.00%) 2
Body tinea subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	1 / 20 (5.00%) 1	0 / 40 (0.00%) 0
Cystitis subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	1 / 20 (5.00%) 1	0 / 40 (0.00%) 0
Fungal skin infection subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	1 / 20 (5.00%) 1	0 / 40 (0.00%) 0
Influenza subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	1 / 20 (5.00%) 1	0 / 40 (0.00%) 0
Lower respiratory tract infection subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0	1 / 20 (5.00%) 1	0 / 40 (0.00%) 0
Otitis externa			

subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Periodontitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 42 (0.00%)	1 / 20 (5.00%)	1 / 40 (2.50%)
occurrences (all)	0	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 April 2022	<p>28. GSI Grading Scale for Severity of Adverse Events and Laboratory Abnormalities: Text was added to clarify that IRRs will be graded based on Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0.</p> <p>29. Text was added to clarify that management of toxicity considered related to nivolumab must follow the toxicity management guidance as outlined in the local label for nivolumab.</p>
20 April 2022	<p>Amendment 1: 1. The ClinicalTrials.gov identifier is available.</p> <p>2. Text was added to clarify that this study will be conducted in compliance with this protocol and in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) and applicable regulatory requirements.</p> <p>3. Text was added to provide updated information on drug-drug interaction data for SLGN and acid-reducing agents.</p> <p>4. Text was updated to provide a consistent endpoint irrespective of the different assay limits of detection.</p> <p>5. Text was updated to clarify the definition of virologic breakthrough.</p> <p>6. Text was updated to clarify the definition of virologic breakthrough.</p> <p>7. Study design was updated to adjust the proportion of HBeAg-positive and HBeAg-negative participants per cohort.</p> <p>8. Text was updated to include alanine aminotransferase (ALT) values for discontinuation criteria and the rationale for allowing discontinuation of study drug at end of treatment (EOT) even if the criteria specified are not met and to specify additional discontinuation criteria.</p> <p>9. Exclusion criteria were updated to reduce the time from screening for liver biopsy and FibroScan test so that these results could be used for exclusion criteria, and to include details for excluding participants in Cohorts 2 and 3 who fall under the standard of care indication.</p> <p>10. Nivolumab administration duration was updated.</p> <p>11. Text was added to clarify that coadministration of antiemetic medication was allowed at the discretion of the investigator and to align with Gilead's guidance for concomitant medication for COVID-19 vaccines.</p> <p>12. Text was updated to allow acid-reducing agents.</p> <p>13. Text was updated to allow for remote drug accountability review.</p>

20 April 2022	<p>14. Text was updated to add sparse pharmacokinetics (PK) sampling for nivolumab, and to clarify that sparse PK for SLGN and nivolumab is not required on Day 1 for Cohort 1 and Cohort 2 Group A.</p> <p>15. Text was added to clarify that participants may be asked to consent to HBeAg testing prior to screening procedures in order to ensure the required minimum of 20% HBeAg-positive participants for each cohort.</p> <p>16. Screening visit: Text was updated to extend the screening window to 45 days.</p> <p>17. Baseline/Day 1 Assessments: Text was updated to extend the screening window to 45 days.</p> <p>18. Criteria were updated to align discontinuation criteria based on Grade 3 or Grade 4 adverse events or laboratory abnormalities. Additional criteria were added to define parameters for permanent discontinuation of study treatment in the event of hepatic disease progression and/or lack of efficacy.</p> <p>19. Text was added to clarify the process for premature study discontinuation.</p> <p>20. Assessment of Severity: Text was updated to clarify that grading of infusion-related reaction (IRRs) will be done according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0.</p> <p>21. Text was updated to clarify the definition of hepatotoxicity.</p> <p>22. ALT Elevation or Flare Management on Treatment and Treatment-Free Follow-up: Text was updated to provide a consistent endpoint irrespective of the different assay limits of detection.</p> <p>23. Primary Endpoint: Text was updated to provide a consistent endpoint irrespective of the different assay limits of detection.</p> <p>24. Text was updated to specify plasma vs serum PK.</p> <p>25. Text was updated to align with Gilead's template language for case report forms.</p> <p>26. Text was updated to provide clarification on the preparation of study reports and Gilead publication policies.</p> <p>27. Study Drug Effects on Pregnancy and Hormonal Contraception was updated for VIR-2218, as per the latest investigator's brochure.</p>
12 April 2023	<p>15. FU Week 2 was removed in order to simplify the FU period for participants.</p> <p>16. References to Cohort 3 were removed throughout the protocol due to the decision to discontinue this cohort.</p> <p>17. Incidences of Global Patient Safety have been changed to Patient Safety (PS).</p> <p>18. Minor changes included to correct typographical errors.</p>
12 April 2023	<p>Amendment 2: 1. References to nivolumab were modified throughout the protocol due to Gilead's decision to discontinue nivolumab dosing across study cohorts.</p> <p>2. An ongoing study (GS-US-389-5458) assessing the safety, tolerability and efficacy of once-weekly administration of SLGN 3 mg in special populations with chronic hepatitis B virus (CHB) was added.</p> <p>3. Figure 1 was updated in order to reflect the current changes to study design.</p> <p>4. A new section to describe the rationale for modifications to the study design was added following the decision to discontinue nivolumab dosing.</p> <p>5. Benefit/Risk Assessment for nivolumab and Overall Benefit/Risk was updated following discontinuation of nivolumab in this study.</p> <p>6. Number of viremic chronic hepatitis B (CHB)-infected participants was reduced from 80 to 60 participants to reflect a prior sponsor decision that cohort 3 would not be enrolled.</p> <p>7. A new subsection for changes to the study design was added.</p> <p>8. All incidences of 'Participants who remain on nucleos(t)ide (NUC) treatment into follow-up (FU) period are not required to attend follow up FU Weeks 2 and 8 visits' have been removed as all participants in Cohort 1 will remain on NUCs throughout the FU period.</p> <p>9. FU period was updated to outline the procedures following the change to study design.</p> <p>10. An individual treatment modification criterion (Any on treatment uveitis, confirmed by ophthalmologic evaluation) was moved to individual treatment discontinuation criteria after confirmation that no rechallenge was required following the resolution of the AE.</p> <p>11. A new section for toxicity management of irAEs observed with nivolumab was added.</p> <p>12. AE of special interest (eg, uveitis) was added to the safety analysis.</p> <p>13. FU Week 8 virtual/telephonic visit pregnancy test was changed across all cohorts.</p> <p>14. The visit windows for FU Weeks 24 through FU Week 48 (for Cohorts 1 and 2) were extended to ± 14 days.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported