Clinical trial results:
A Phase 3, Randomized, Double-Blind Study to Evaluate the Efficacy and Safety of Switching from Tenofovir Disoproxil Fumarate (TDF) 300 mg QD to Tenofovir Alafenamide (TAF) 25mg QD in Subjects with Chronic Hepatitis B who are Virologically Suppressed

Summary

EudraCT number	2016-003632-20
Trial protocol	GB ES IT
Global end of trial date	30 January 2020

Results information

Result version number	v1 (current)
This version publication date	09 September 2020
First version publication date	09 September 2020

Trial information

Trial identification

Sponsor protocol code	GS-US-320-4018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02979613
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	30 January 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 September 2018
Global end of trial reached?	Yes
Global end of trial date	30 January 2020
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 efficacy, safety, and tolerability of switching to tenofovir alafenamide (TAF) versus continuing tenofovir disoproxil fumarate (TDF) in virologically suppressed adults with chronic hepatitis B virus (HBV) infection.

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	29 December 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 138
Country: Number of subjects enrolled	United States: 128
Country: Number of subjects enrolled	Canada: 89
Country: Number of subjects enrolled	Taiwan: 41
Country: Number of subjects enrolled	Spain: 31
Country: Number of subjects enrolled	Hong Kong: 28
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	United Kingdom: 14
Worldwide total number of subjects	490
EEA total number of subjects	66

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)	440
From 65 to 84 years	50
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in North America, Europe, and Asia. The first participant was screened on 29 December 2016. The last study visit occurred on 30 January 2020.

Pre-assignment

Screening details:

541 participants were screened.

Period 1

Period 1 title	Double-Blind (DB) Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	TAF 25 mg

Arm description:

Participants who were virologically suppressed and taking TDF 300 mg tablet orally once daily received TAF 25 mg tablet orally once daily, and placebo to match TDF once daily for up to 53 weeks in the DB phase. Participants who completed DB treatment and were willing to enter in the open-label extension (OLE) phase, received TAF 25 mg tablet orally once daily for up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	TAF
Investigational medicinal product code	
Other name	Vemlidy®, GS-7340
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg administered once daily for 53 weeks.

Investigational medicinal product name	TDF placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

TDF matched placebo administered once daily for 53 weeks.

Arm title	TDF 300 mg

Arm description:

Participants who were virologically suppressed and taking TDF 300 mg tablet orally once daily received TDF 300 mg tablet orally once daily, and placebo to match TAF once daily for up to 50 weeks in the DB phase. Participants who completed DB treatment and were willing to enter in the OLE phase, received TAF 25 mg tablet orally once daily for up to 52 weeks.

Arm type	Active comparator
Investigational medicinal product name	TDF
Investigational medicinal product code	
Other name	Viread®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: 300 mg administered once daily for 50 weeks.	
Investigational medicinal product name	TAF placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: TAF matched placebo administered once daily for 50 weeks.	

Number of subjects in period 1[1]	TAF 25 mg	TDF 300 mg
Started	243	245
Completed	235	237
Not completed	8	8
Withdrew Consent	2	4
Adverse Event	2	-
Pregnancy	2	2
Protocol Violation	1	1
Lost to follow-up	1	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: Two participants who were randomised but did not receive the study drug are not included in the subject disposition table.

Period 2

Period 2 title	Open-Label Extension (OLE) Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	TAF 25 mg

Arm description:

Participants who were virologically suppressed and taking TDF 300 mg tablet orally once daily received TAF 25 mg tablet orally once daily, and placebo to match TDF once daily for up to 53 weeks in the DB phase. Participants who completed DB treatment and were willing to enter in the OLE phase, received TAF 25 mg tablet orally once daily for up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	TAF
Investigational medicinal product code	
Other name	Vemlidy®, GS-7340
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 25 mg administered once daily for 52 weeks.	

Arm title	TDF 300 mg

Arm description:

Participants who were virologically suppressed and taking TDF 300 mg tablet orally once daily received TDF 300 mg tablet orally once daily, and placebo to match TAF once daily for up to 50 weeks in the DB phase. Participants who completed DB treatment and were willing to enter in the OLE phase, received TAF 25 mg tablet orally once daily for up to 52 weeks.

Arm type	Active comparator
Investigational medicinal product name	TAF
Investigational medicinal product code	
Other name	Vemlidy®, GS-7340
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg administered once daily for 52 weeks.

Number of subjects in period 2	TAF 25 mg	TDF 300 mg
Started	235	237
Completed	232	231
Not completed	3	6
Withdrew Consent	2	4
Adverse Event	1	-
Death	-	1
Investigator's Discretion	-	1

Baseline characteristics

Reporting groups	
Reporting group title	TAF 25 mg
Reporting group description:	
Participants who were virologically suppressed and taking TDF 300 mg tablet orally once daily received TAF 25 mg tablet orally once daily, and placebo to match TDF once daily for up to 53 weeks in the DB phase. Participants who completed DB treatment and were willing to enter in the open-label extension (OLE) phase, received TAF 25 mg tablet orally once daily for up to 52 weeks.	
Reporting group title	TDF 300 mg
Reporting group description:	
Participants who were virologically suppressed and taking TDF 300 mg tablet orally once daily received TDF 300 mg tablet orally once daily, and placebo to match TAF once daily for up to 50 weeks in the DB phase. Participants who completed DB treatment and were willing to enter in the OLE phase, received TAF 25 mg tablet orally once daily for up to 52 weeks.	

Reporting group values	TAF 25 mg	TDF 300 mg	Total
Number of subjects	243	245	488
Age categorical Units: Subjects			
< 50 Years	107	109	216
≥ 50 Years	136	136	272
Age continuous Units: years			
arithmetic mean	51.0	51.0	
standard deviation	± 10.5	± 10.8	-
Gender categorical Units: Subjects			
Female	64	79	143
Male	179	166	345
Race Units: Subjects			
Asian	195	205	400
Black or African American	9	8	17
Native Hawaiian or Pacific Islander	0	1	1
White	38	31	69
Other	1	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	3	0	3
Not Hispanic or Latino	240	245	485
Unknown or Not Reported	0	0	0
ALT Level Based on Central Lab Normal Range			
Measure Description: Central laboratory upper limit of normal (ULN) for ALT were as follows: ≤ 43 U/L for males aged 18 to < 69 years and ≤ 35 U/L for males aged ≥ 69 years; ≤ 34 U/L for females aged 18 to < 69 years and ≤ 32 U/L for females aged ≥ 69 years.			
Units: Subjects			
≤ ULN	211	226	437
> ULN to 5xULN	32	19	51
> 5xULN	0	0	0

ALT Level Based on 2018 American Association for the Study of Liver Diseases (AASLD) Normal Range			
The ULN for ALT using the 2018 AASLD normal range was 25 U/L for females and 35 U/L for males.			
Units: Subjects			
≤ ULN	191	192	383
> ULN to 5xULN	52	53	105
> 5xULN	0	0	0
Hepatitis B virus (HBV) DNA Category Units: Subjects			
< 20 IU/mL	238	242	480
20 to < 69 IU/mL	2	3	5
≥ 69 IU/mL	3	0	3
Hepatitis B e Antigen/Antibody (HBeAg/HBeAb) Status			
HBeAb status was imputed as negative if missing.			
Units: Subjects			
Positive/Negative	78	78	156
Positive/Positive	0	1	1
Negative/Negative	17	28	45
Negative/Positive	148	138	286
Hip Bone Mineral Density (BMD) Status			
Hip Dual-Energy X-Ray Absorptiometry (DXA) Analysis Set included all participants who were randomized into the study, received at least 1 dose of study drug, and had nonmissing baseline hip BMD values.			
Units: Subjects			
Normal (T-score ≥ -1.0)	143	124	267
Osteopenia (-2.5 ≤ T-score < -1.0)	89	116	205
Osteoporosis (T-score < -2.5)	9	4	13
No Data Collected	2	1	3
Spine BMD Status			
Spine DXA Analysis Set included all participants who were randomized into the study, received at least 1 dose of study drug, and had nonmissing baseline spine BMD values.			
Units: Subjects			
Normal (T-score ≥ -1.0)	125	120	245
Osteopenia (-2.5 ≤ T-score < -1.0)	90	97	187
Osteoporosis (T-score < -2.5)	28	28	56
Alanine Aminotransferase (ALT) Units: U/L			
arithmetic mean	28.0	26.0	
standard deviation	± 15.6	± 12.0	-
FibroTest® Score			
The FibroTest® score is used to assess liver fibrosis. Scores range from 0.00 to 1.00, with higher scores indicating a greater degree of fibrosis. Participants in the Safety Analysis Set with available data were analyzed (N = 241, 245).			
Units: score on a scale			
arithmetic mean	0.42	0.41	
standard deviation	± 0.234	± 0.211	-
Estimated Glomerular Filtration Rate by the Cockcroft-Gault Formula (eGFR-CG) Units: mL/min			
arithmetic mean	95.0	93.8	
standard deviation	± 25.58	± 25.16	-

End points

End points reporting groups

Reporting group title	TAF 25 mg

Reporting group description:

Participants who were virologically suppressed and taking TDF 300 mg tablet orally once daily received TAF 25 mg tablet orally once daily, and placebo to match TDF once daily for up to 53 weeks in the DB phase. Participants who completed DB treatment and were willing to enter in the open-label extension (OLE) phase, received TAF 25 mg tablet orally once daily for up to 52 weeks.

Reporting group title	TDF 300 mg

Reporting group description:

Participants who were virologically suppressed and taking TDF 300 mg tablet orally once daily received TDF 300 mg tablet orally once daily, and placebo to match TAF once daily for up to 50 weeks in the DB phase. Participants who completed DB treatment and were willing to enter in the OLE phase, received TAF 25 mg tablet orally once daily for up to 52 weeks.

Reporting group title	TAF 25 mg

Reporting group description:

Participants who were virologically suppressed and taking TDF 300 mg tablet orally once daily received TAF 25 mg tablet orally once daily, and placebo to match TDF once daily for up to 53 weeks in the DB phase. Participants who completed DB treatment and were willing to enter in the OLE phase, received TAF 25 mg tablet orally once daily for up to 52 weeks.

Reporting group title	TDF 300 mg

Reporting group description:

Participants who were virologically suppressed and taking TDF 300 mg tablet orally once daily received TDF 300 mg tablet orally once daily, and placebo to match TAF once daily for up to 50 weeks in the DB phase. Participants who completed DB treatment and were willing to enter in the OLE phase, received TAF 25 mg tablet orally once daily for up to 52 weeks.

Primary: Percentage of Participants With Hepatitis B Virus (HBV) DNA Levels ≥ 20 IU/mL at Week 48, as Determined by the Modified United States Food and Drug Administration (US FDA)-Defined Snapshot Algorithm

End point title	Percentage of Participants With Hepatitis B Virus (HBV) DNA Levels ≥ 20 IU/mL at Week 48, as Determined by the Modified United States Food and Drug Administration (US FDA)-Defined Snapshot Algorithm

End point description:

The percentage of participants with HBV DNA ≥ 20 IU/mL at Week 48 was analyzed using the modified US FDA-defined snapshot algorithm, which included participants who:
1. Had the last available on-treatment HBV DNA ≥ 20 IU/mL in the Week 48 analysis window (from Day 295 to Day 378, inclusive), or
2. Did not have on-treatment HBV DNA data available in the Week 48 analysis window and
- Discontinued study drug prior to or in the Week 48 analysis window due to lack of efficacy, or
- Discontinued study drug prior to or in the Week 48 analysis window due to reason other than lack of efficacy and had the last available on-treatment HBV DNA ≥ 20 IU/mL.

The Full Analysis Set included all participants who were randomized into the study and received at least 1 dose of study drug. Participants were analyzed according to the treatment to which they were randomized.

End point type	Primary

End point timeframe:

Week 48

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	245		
Units: percentage of participants				
number (not applicable)	0.4	0.4		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg

Statistical analysis description:

The null hypothesis was that the TAF group is at least 4% worse than the TDF group with respect to the percentage of participants with HBV DNA ≥ 20 IU/mL at Week 48. The alternative hypothesis was that the TAF group is less than 4% worse than the TDF group with respect to the percentage of participants with HBV DNA ≥ 20 IU/mL at Week 48.

Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in the Percentages
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	2

Secondary: Percentage of Participants With HBV DNA Levels ≥ 20 IU/mL at Week 96, as Determined by the Modified US FDA-Defined Snapshot Algorithm

End point title	Percentage of Participants With HBV DNA Levels ≥ 20 IU/mL at Week 96, as Determined by the Modified US FDA-Defined Snapshot Algorithm

End point description:

The percentage of participants with HBV DNA ≥ 20 IU/mL at Week 96 was analyzed using the modified US FDA-defined snapshot algorithm, which included participants who:
1. Had the last available on-treatment HBV DNA ≥ 20 IU/mL in the Week 96 analysis window (from Day 589 to Day 840, inclusive), or
2. Did not have on-treatment HBV DNA data available in the Week 96 analysis window and
-Discontinued study drug prior to or in the Week 96 analysis window due to lack of efficacy, or
-Discontinued study drug prior to or in the Week 96 analysis window due to reason other than lack of efficacy and had the last available on-treatment HBV DNA ≥ 20 IU/mL.
Participants in the Full Analysis Set were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 96

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	245		
Units: percentage of participants				
number (not applicable)	0.4	0.4		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in the Percentages
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	1.9

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9953 [1]
Method	Cochran-Mantel-Haenszel

Notes:

[1] - P-value for the superiority tests compared the percentage of each HBV DNA outcome was from CMH tests stratified by baseline age groups and baseline HBeAg status strata.

Secondary: Percentage of Participants With HBV DNA Levels < 20 IU/mL at Week 48

End point title	Percentage of Participants With HBV DNA Levels < 20 IU/mL at Week 48

End point description:

The percentage of participants with HBV DNA < 20 IU/mL at Week 48 was analyzed, which included participants who have the last available on-treatment HBV DNA, 20 IU/mL in the Week 48 analysis window. Missing=Failure (M = F) approach was used for analysis. Participants in the Full Analysis Set were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 48

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	245		
Units: percentage of participants				
number (not applicable)	96.3	96.3		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in the Percentages
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	3.7

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.98 [2]
Method	Cochran-Mantel-Haenszel

Notes:

[2] - P-value for the superiority tests compared the percentage of each HBV DNA outcome was from CMH tests stratified by baseline age groups and baseline HBeAg status strata.

Secondary: Percentage of Participants With HBV DNA Levels < 20 IU/mL (Target Detected/Not Detected) at Week 48

End point title	Percentage of Participants With HBV DNA Levels < 20 IU/mL (Target Detected/Not Detected) at Week 48

End point description:

The percentage of participants with HBV DNA < 20 IU/mL at Week 48 was analyzed, which included participants who have the last available on-treatment HBV DNA, 20 IU/mL in the Week 48 analysis window. The method of determining percentage of participants with HBV DNA levels <20 IU/mL (target detected/not detected i.e., lower limit of detection) at Week 48, was handled by M = F, and Missing=Excluded (M = E) approaches. Participants in the Full Analysis Set were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 48

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	245		
Units: percentage of participants				
number (not applicable)				
M = F Approach: < 20 IU/mL Target Not Detected	63.4	62.0		
M = F Approach: < 20 IU/mL Target Detected	32.9	34.3		
M = E Approach: < 20 IU/mL Target Not Detected	65.5	64.1		
M = E Approach: < 20 IU/mL Target Detected	34.0	35.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HBV DNA Levels < 20 IU/mL at Week 96

End point title	Percentage of Participants With HBV DNA Levels < 20 IU/mL at Week 96

End point description:

The percentage of participants with HBV DNA < 20 IU/mL at Week 96 was analyzed, which included participants who have the last available on-treatment HBV DNA, 20 IU/mL in the Week 96 analysis window. M = F approach was used for analysis. Participants in the Full Analysis Set were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 96

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	245		
Units: percentage of participants				
number (not applicable)	94.7	93.9		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg

Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in the Percentages
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	5.2

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6863 [3]
Method	Cochran-Mantel-Haenszel

Notes:

[3] - P-value for the superiority tests compared the percentage of each HBV DNA outcome was from CMH tests stratified by baseline age groups and baseline HBeAg status strata.

Secondary: Percentage of Participants With HBV DNA Levels < 20 IU/mL (Target Detected/Not Detected) at Week 96, as Determined by the Modified US FDA-Defined Snapshot Algorithm

End point title	Percentage of Participants With HBV DNA Levels < 20 IU/mL (Target Detected/Not Detected) at Week 96, as Determined by the Modified US FDA-Defined Snapshot Algorithm

End point description:

The percentage of participants with HBV DNA < 20 IU/mL at Week 96 was analyzed, which included participants who have the last available on-treatment HBV DNA, 20 IU/mL in the Week 96 analysis window. The method of determining percentage of participants with HBV DNA levels <20 IU/mL (target detected/not detected i.e., lower limit of detection) at Week 96, was handled by Missing=Failure (M = F), and Missing=Excluded (M = E) approaches. Participants in the Full Analysis Set were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 96

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	245		
Units: percentage of participants				
number (not applicable)				
M = F Approach: < 20 IU/mL Target Not Detected	65.8	66.1		
M = F Approach: < 20 IU/mL Target Detected	28.8	27.8		

M = E Approach: < 20 IU/mL Target Not Detected	69.3	70.1		
M = E Approach: < 20 IU/mL Target Detected	30.3	29.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Hepatitis B e Antigen (HBeAg) Loss at Week 48

End point title	Percentage of Participants With Hepatitis B e Antigen (HBeAg) Loss at Week 48

End point description:

HBeAg loss was defined as HBeAg changing from positive at baseline to negative at a postbaseline visit with baseline HBeAb negative or missing. The M = F approach was used for this analysis. The Serologically Evaluable Full Analysis Set for HBeAg loss and seroconversion included all participants who were randomized and received at least 1 dose of study drug and were HBeAg-positive and HBeAb-negative or had a missing value at baseline. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 48

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	78		
Units: percentage of participants				
number (not applicable)	7.7	6.4		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7258 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	10.1

Notes:

[4] - P-value was from the CMH test, stratified by baseline age groups (< 50, ≥ 50 years).

Secondary: Percentage of Participants With HBeAg Seroconversion at Week 48

End point title	Percentage of Participants With HBeAg Seroconversion at Week 48

End point description:

HBeAg seroconversion was defined as HBeAg loss and HBeAb changing from negative/missing at baseline to positive at a postbaseline visit. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBeAg loss and seroconversion were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 48

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	78		
Units: percentage of participants				
number (not applicable)	2.6	0.0		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1348 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	7.7

Notes:

[5] - P-value was from the CMH test, stratified by baseline age groups (< 50, ≥ 50 years).

Secondary: Percentage of Participants With HBeAg Loss at Week 96

End point title	Percentage of Participants With HBeAg Loss at Week 96

End point description:

HBeAg loss was defined as HBeAg changing from positive at baseline to negative at a postbaseline visit with baseline HBeAb negative or missing. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBeAg loss and seroconversion were analyzed.

Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 96

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	78		
Units: percentage of participants				
number (not applicable)	17.9	9.0		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1005 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	20.1

Notes:

[6] - P-value was from CMH tests stratified by baseline age groups (< 50, ≥ 50 years).

Secondary: Percentage of Participants With HBeAg Seroconversion at Week 96

End point title	Percentage of Participants With HBeAg Seroconversion at Week 96

End point description:

HBeAg seroconversion was defined as HBeAg loss and HBeAb changing from negative/missing at baseline to positive at a postbaseline visit. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBeAg loss and seroconversion were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 96

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	78		
Units: percentage of participants				
number (not applicable)	5.1	2.6		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4154 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	9.5

Notes:

[7] - P-value was from CMH tests stratified by baseline age groups (< 50, ≥ 50 years).

Secondary: Percentage of Participants With Hepatitis B Surface Antigen (HBsAg) Loss at Week 48

End point title	Percentage of Participants With Hepatitis B Surface Antigen (HBsAg) Loss at Week 48

End point description:

HBsAg loss was defined as HBsAg changing from positive at baseline to negative at a postbaseline visit with baseline HBsAb negative or missing. The M = F approach was used for this analysis. The Serologically Evaluable Full Analysis Set for HBsAg loss and seroconversion included all participants who were randomized and received at least 1 dose of study drug and were HBsAg-positive and HBsAb-negative or had a missing value at baseline. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 48

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	245		
Units: percentage of participants				
number (not applicable)	0.0	2.0		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0281 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	0.3

Notes:

[8] - P-value was from the CMH test, stratified by baseline age groups (< 50, ≥ 50 years) and baseline HBeAg status strata.

Secondary: Percentage of Participants With HBsAg Seroconversion at Week 48

End point title	Percentage of Participants With HBsAg Seroconversion at Week 48

End point description:

HBsAg seroconversion was defined as HBsAg loss and HBsAb changes from negative/missing at baseline to positive at a postbaseline visit. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBsAg loss and seroconversion were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 48

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	245		
Units: percentage of participants				
number (not applicable)	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HBsAg Loss at Week 96

End point title	Percentage of Participants With HBsAg Loss at Week 96

End point description:

HBsAg loss was defined as HBsAg changing from positive at baseline to negative at a postbaseline visit with baseline HBsAb negative or missing. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBsAg loss and seroconversion were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 96

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	245		
Units: percentage of participants				
number (not applicable)	1.6	2.4		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5373 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	2.1

Notes:

[9] - P-value was from CMH tests stratified by baseline age groups (< 50, ≥ 50 years) and baseline HBeAg status strata.

Secondary: Percentage of Participants With HBsAg Seroconversion at Week 96

End point title	Percentage of Participants With HBsAg Seroconversion at Week 96

End point description:

HBsAg seroconversion was defined as HBsAg loss and HBsAb changes from negative/missing at baseline to positive at a postbaseline visit. The M = F approach was used for this analysis. Participants in the Serologically Evaluable Full Analysis Set for HBsAg loss and seroconversion were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 96

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	245		
Units: percentage of participants				
number (not applicable)	0.8	0.4		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5845 [10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	2.5

Notes:

[10] - P-value was from CMH tests stratified by baseline age groups (< 50, ≥ 50 years) and baseline HBeAg status strata.

Secondary: Percentage of Participants With Normal Alanine Aminotransferase (ALT) at Week 48 (by Central Laboratory and the American Association for the Study of Liver Diseases [AASLD] Criteria)

End point title	Percentage of Participants With Normal Alanine Aminotransferase (ALT) at Week 48 (by Central Laboratory and the American Association for the Study of Liver Diseases [AASLD] Criteria)

End point description:

Central laboratory ULN for ALT were as follows: ≤ 43 U/L for males aged 18 to < 69 years and ≤ 35 U/L for males aged ≥ 69 years; ≤ 34 U/L for females aged 18 to < 69 years and ≤ 32 U/L for females aged ≥ 69 years. The ULN for ALT using the 2018 AASLD normal range was 25 U/L for females and 35 U/L for males. M = F approach was used for analysis. Participants in the Full Analysis Set were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 48

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	245		
Units: percentage of participants				
number (not applicable)				
Central Laboratory Criteria	89.3	84.9		
AASLD Criteria	79.0	75.1		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Statistical analysis description:	
Central Laboratory Criteria	
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1405 [11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	10.6

Notes:

[11] - P-value was from the CMH test, stratified by baseline age groups (< 50, ≥ 50 years) and baseline HBeAg status strata.

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Statistical analysis description:	
AASLD Criteria	
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3133 [12]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	11.4

Notes:

[12] - P-value was from the CMH test, stratified by baseline age groups (< 50, ≥ 50 years) and baseline HBeAg status strata.

Secondary: Percentage of Participants With Normalized ALT at Week 48 (by Central Laboratory and AASLD Criteria)

End point title	Percentage of Participants With Normalized ALT at Week 48 (by Central Laboratory and AASLD Criteria)

End point description:

ALT normalization was defined as an ALT value that changed from above the normal range at baseline to within the normal range at the given postbaseline visit. Central laboratory ULN for ALT were as follows: ≤ 43 U/L for males aged 18 to < 69 years and ≤ 35 U/L for males aged ≥ 69 years; ≤ 34 U/L for females aged 18 to < 69 years and ≤ 32 U/L for females aged ≥ 69 years. The ULN for ALT using the 2018 AASLD normal range was 25 U/L for females and 35 U/L for males. M = F approach was used for analysis. Participants in the Full Analysis Set with Baseline ALT > ULN were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 48

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	53		
Units: percentage of participants				
number (not applicable)				
Central Laboratory Criteria (N = 32, 19)	50.0	36.8		
AASLD Criteria	50.0	26.4		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg

Statistical analysis description:

Central Laboratory Criteria

Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3381 [13]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	14.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.4
upper limit	44.6

Notes:

[13] - P-value was from the CMH test, stratified by baseline age groups (< 50, ≥ 50 years) and baseline HBeAg status strata.

Statistical analysis title	TAF 25 mg vs TDF 300 mg

Statistical analysis description:	
AASLD Criteria	
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0136 [14]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	23.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.3
upper limit	42.3

Notes:

[14] - P-value was from the CMH test, stratified by baseline age groups (< 50, ≥ 50 years) and baseline HBeAg status strata.

Secondary: Percentage of Participants With Normal ALT at Week 96 (by Central Laboratory and the AASLD Criteria)

End point title	Percentage of Participants With Normal ALT at Week 96 (by Central Laboratory and the AASLD Criteria)

End point description:

Central laboratory ULN for ALT were as follows: ≤ 43 U/L for males aged 18 to < 69 years and ≤ 35 U/L for males aged ≥ 69 years; ≤ 34 U/L for females aged 18 to < 69 years and ≤ 32 U/L for females aged ≥ 69 years. The ULN for ALT using the 2018 AASLD normal range was 25 U/L for females and 35 U/L for males. M = F approach was used for analysis. Participants in the Full Analysis Set were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 96

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	245		
Units: percentage of participants				
number (not applicable)				
Central Laboratory Criteria	88.5	91.4		
AASLD Criteria	80.7	86.5		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Statistical analysis description:	
Central Laboratory Criteria	
Comparison groups	TAF 25 mg v TDF 300 mg

Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2803 [15]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	2.6

Notes:

[15] - P-value was from CMH tests stratified by baseline age groups (< 50, ≥ 50 years) and baseline HBeAg status strata.

Statistical analysis title	TAF 25 mg vs TDF 300 mg

Statistical analysis description:

AASLD Criteria

Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0788 [16]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	-5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.6
upper limit	0.7

Notes:

[16] - P-value was from CMH tests stratified by baseline age groups (< 50, ≥ 50 years) and baseline HBeAg status strata.

Secondary: Percentage of Participants With Normalized ALT at Week 96 (by Central Laboratory and AASLD Criteria)

End point title	Percentage of Participants With Normalized ALT at Week 96 (by Central Laboratory and AASLD Criteria)

End point description:

ALT normalization was defined as an ALT value that changed from above the normal range at baseline to within the normal range at the given postbaseline visit. Central laboratory ULN for ALT were as follows: ≤ 43 U/L for males aged 18 to < 69 years and ≤ 35 U/L for males aged ≥ 69 years; ≤ 34 U/L for females aged 18 to < 69 years and ≤ 32 U/L for females aged ≥ 69 years. The ULN for ALT using the 2018 AASLD normal range was 25 U/L for females and 35 U/L for males. M = F approach was used for analysis. Participants in the Full Analysis Set with Baseline ALT > ULN were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Week 96

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	53		
Units: percentage of participants				
number (not applicable)				
Central Laboratory Criteria (N = 32, 19)	56.3	78.9		
AASLD Criteria	55.8	73.6		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Statistical analysis description:	
Central Laboratory Criteria	
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.088 [17]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	-23.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51.2
upper limit	3.4

Notes:

[17] - P-value was from CMH tests stratified by baseline age groups (< 50, ≥ 50 years) and baseline HBeAg status strata.

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Statistical analysis description:	
AASLD Criteria	
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.051 [18]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in the Percentages
Point estimate	-18.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.4
upper limit	0.2

Notes:

[18] - P-value was from CMH tests stratified by baseline age groups (< 50, ≥ 50 years) and baseline HBeAg status strata.

Secondary: Change From Baseline in FibroTest® Score at Week 48

End point title	Change From Baseline in FibroTest® Score at Week 48

End point description:

The FibroTest score is used to assess liver fibrosis. Scores range from 0.00 to 1.00, with higher scores indicating a greater degree of fibrosis. Change from baseline was calculated as the value at Week 48 minus the value at Baseline. Participants in the Full Analysis Set with available data were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	236		
Units: score on a scale				
arithmetic mean (standard deviation)	-0.02 (± 0.082)	-0.01 (± 0.082)		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg

Statistical analysis description:

P-value, difference in least squares mean (LSM), and its 95% CI were derived from analysis of variance (ANOVA) model with baseline age groups (< 50, ≥ 50 years), baseline HBeAg status, and treatment group as fixed effects in the model.

Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	470
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0186
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0

Secondary: Change From Baseline in FibroTest® Score at Week 96

End point title	Change From Baseline in FibroTest® Score at Week 96

End point description:

The FibroTest score is used to assess liver fibrosis. Scores range from 0.00 to 1.00, with higher scores indicating a greater degree of fibrosis. Change from baseline was calculated as the value at Week 96 minus the value at Baseline. Participants in the Full Analysis Set with available data were analyzed. Participants were analyzed according to the treatment to which they were randomized.

End point type	Secondary
End point timeframe:	
Baseline; Week 96	

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	232		
Units: score on a scale				
arithmetic mean (standard deviation)	-0.03 (± 0.080)	-0.03 (± 0.090)		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Statistical analysis description:	
P-value, difference in LSM, and its 95% CI were from ANOVA with baseline age groups (<50, ≥ 50 years), baseline HBeAg status, and treatment group as fixed effects in the model.	
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	463
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6956
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.01

Secondary: Percent Change From Baseline in Hip Bone Mineral Density (BMD) at Week 48

End point title	Percent Change From Baseline in Hip Bone Mineral Density (BMD) at Week 48
End point description:	
Percent Change = Change from baseline at a postbaseline visit/baseline * 100%. Participants in the Hip DXA Analysis Set (included all participants who were randomized into the study, received at least 1 dose of study drug, and had non-missing baseline hip BMD values) with available data were analysed. Participants were analyzed according to the treatment they actually received.	
End point type	Secondary
End point timeframe:	
Baseline; Week 48	

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	226		
Units: percent change				
arithmetic mean (standard deviation)	0.659 (± 2.0818)	-0.507 (± 1.9051)		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Statistical analysis description:	
P-value, difference in LSM, and its 95% CI were from ANOVA with baseline age groups (<50, ≥ 50 years), baseline HBeAg status, and treatment group as fixed effects in the model.	
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	451
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	1.167
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.797
upper limit	1.536

Secondary: Percent Change From Baseline in Hip BMD at Week 96

End point title	Percent Change From Baseline in Hip BMD at Week 96
End point description:	
Percent Change = Change from baseline at a postbaseline visit/baseline * 100%. Participants in the Hip DXA Analysis Set with available data were analyzed. Participants were analyzed according to the treatment they actually received.	
End point type	Secondary
End point timeframe:	
Baseline; Week 96	

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	224		
Units: percent change				
arithmetic mean (standard deviation)	1.157 (± 2.8501)	0.180 (± 2.6813)		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Statistical analysis description:	
P-value, difference in LSM, and its 95% CI were from ANOVA with baseline age groups (<50, ≥ 50 years), baseline HBeAg status, and treatment group as fixed effects in the model.	
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	451
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	0.977
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.465
upper limit	1.49

Secondary: Percent Change From Baseline in Spine BMD at Week 48

End point title	Percent Change From Baseline in Spine BMD at Week 48
End point description:	
Percent Change = Change from baseline at a postbaseline visit/baseline * 100%. Participants in the Spine DXA Analysis Set (included all participants who were randomized into the study, received at least 1 dose of study drug, and had non-missing baseline spine BMD values) with available data were analysed. Participants were analyzed according to the treatment they actually received.	
End point type	Secondary
End point timeframe:	
Baseline; Week 48	

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	229		
Units: percent change				
arithmetic mean (standard deviation)	1.743 (± 3.4674)	-0.138 (± 3.1072)		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Statistical analysis description:	
P-value, difference in LSM, and its 95% CI were from ANOVA with baseline age groups (<50, ≥ 50 years), baseline HBeAg status, and treatment group as fixed effects in the model.	
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	456
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	1.881
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.275
upper limit	2.486

Secondary: Percent Change From Baseline in Spine BMD at Week 96

End point title	Percent Change From Baseline in Spine BMD at Week 96
End point description:	
Percent Change = Change from baseline at a postbaseline visit/baseline * 100%. Participants in the Spine DXA Analysis Set with available data were analyzed. Participants were analyzed according to the treatment they actually received.	
End point type	Secondary
End point timeframe:	
Baseline; Week 96	

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	227		
Units: percent change				
arithmetic mean (standard deviation)	2.330 (± 3.9301)	1.726 (± 3.8224)		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg

Statistical analysis description:

P-value, difference in LSM, and its 95% CI were from ANOVA with baseline age groups (<50, ≥ 50 years), baseline HBeAg status, and treatment group as fixed effects in the model.

Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	456
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.097
Method	ANOVA
Parameter estimate	Difference in LSM
Point estimate	0.604
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	1.317

Secondary: Change From Baseline in Estimated Glomerular Filtration Rate Calculated Using the Cockcroft-Gault Equation (eGFR-CG) at Week 48

End point title	Change From Baseline in Estimated Glomerular Filtration Rate Calculated Using the Cockcroft-Gault Equation (eGFR-CG) at Week 48

End point description:

Cockcroft-Gault formula is as follows:
- For men: Glomerular filtration rate (GFR) = (140 - age in years) * body weight in kg / 72 * serum creatinine (mg/dL)
- For women: GFR = 0.85 * (140 - age in years) * body weight in kg / 72 * serum creatinine (mg/dL)
Change from baseline was calculated as the value at Week 48 minus the value at Baseline. Participants in the Safety Analysis Set (included all randomized participants who received at least 1 dose of study drug) with available data were analyzed. Participants were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Baseline; Week 48

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	237		
Units: mL/min				
median (inter-quartile range (Q1-Q3))	2.240 (-3.957 to 7.704)	-1.722 (-7.020 to 2.634)		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	471
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [19]
Method	Wilcoxon rank sum test

Notes:

[19] - P-values were from the 2-sided Wilcoxon rank sum test to compare the 2 treatment groups.

Secondary: Change From Baseline in eGFR-CG at Week 96

End point title	Change From Baseline in eGFR-CG at Week 96

End point description:

Cockcroft-Gault formula is as follows:
- For men: Glomerular filtration rate (GFR) = (140 - age in years) * body weight in kg / 72 * serum creatinine (mg/dL)
- For women: GFR = 0.85 * (140 - age in years) * body weight in kg / 72 * serum creatinine (mg/dL)
Change from baseline was calculated as the value at Week 96 minus the value at Baseline. Participants in the Safety Analysis Set with available data were analyzed. Participants were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Baseline; Week 96

End point values	TAF 25 mg	TDF 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	232	232		
Units: mL/min				
median (inter-quartile range (Q1-Q3))	1.626 (-4.580 to 6.952)	0.544 (-5.227 to 7.678)		

Statistical analyses

Statistical analysis title	TAF 25 mg vs TDF 300 mg
Comparison groups	TAF 25 mg v TDF 300 mg
Number of subjects included in analysis	464
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7535 [20]
Method	Wilcoxon rank sum test

Notes:

[20] - P-values were from the 2-sided Wilcoxon rank sum test to compare the 2 treatment groups.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-Cause Mortality: First dose date up to 161 weeks (up to approximately 3 years); Adverse Events: First dose date up to the last dose (maximum: 105 weeks) plus 3 days

Adverse event reporting additional description:

The Safety Analysis Set included all randomized participants who received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	TAF 25 mg

Reporting group description:

Adverse events reported in this group occurred during the DB phase. Participants who were virologically suppressed and taking TDF 300 mg tablet orally once daily received TAF 25 mg tablet orally once daily, and placebo to match TDF once daily for up to 53 weeks in the DB phase.

Reporting group title	TDF 300 mg

Reporting group description:

Adverse events reported in this group occurred during the DB phase. Participants who were virologically suppressed and taking TDF 300 mg tablet orally once daily received TDF 300 mg tablet orally once daily, and placebo to match TAF once daily for up to 50 weeks in the DB phase.

Reporting group title	OLE TAF 25 mg From TAF 25 mg

Reporting group description:

Adverse events reported in this group occurred during the OLE phase. Participants who completed TAF treatment in the DB phase and were willing to enter in the OLE phase, received TAF 25 mg tablet orally once daily for up to 52 weeks.

Reporting group title	OLE TAF 25 mg From TDF 300 mg

Reporting group description:

Adverse events reported in this group occurred during the OLE phase. Participants who completed TDF treatment in the DB phase and were willing to enter in the OLE phase, received TAF 25 mg tablet orally once daily for up to 52 weeks.

Serious adverse events	TAF 25 mg	TDF 300 mg	OLE TAF 25 mg From TAF 25 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 243 (4.53%)	3 / 245 (1.22%)	8 / 235 (3.40%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	1 / 243 (0.41%)	1 / 245 (0.41%)	2 / 235 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			

subjects affected / exposed	1 / 243 (0.41%)	0 / 245 (0.00%)	0 / 235 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipoma			
subjects affected / exposed	1 / 243 (0.41%)	0 / 245 (0.00%)	0 / 235 (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
Lung squamous cell carcinoma stage II			
subjects affected / exposed	0 / 243 (0.00%)	0 / 245 (0.00%)	1 / 235 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Testicular neoplasm			
subjects affected / exposed	0 / 243 (0.00%)	0 / 245 (0.00%)	0 / 235 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Muscle rupture			
subjects affected / exposed	1 / 243 (0.41%)	0 / 245 (0.00%)	0 / 235 (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
Tendon injury			
subjects affected / exposed	1 / 243 (0.41%)	0 / 245 (0.00%)	0 / 235 (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
Wrist fracture			
subjects affected / exposed	1 / 243 (0.41%)	0 / 245 (0.00%)	0 / 235 (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
Vascular disorders			
Varicose vein			
subjects affected / exposed	0 / 243 (0.00%)	1 / 245 (0.41%)	0 / 235 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 243 (0.00%)	0 / 245 (0.00%)	0 / 235 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 243 (0.41%)	0 / 245 (0.00%)	0 / 235 (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
Atrial fibrillation			
subjects affected / exposed	0 / 243 (0.00%)	0 / 245 (0.00%)	0 / 235 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 243 (0.00%)	0 / 245 (0.00%)	0 / 235 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 243 (0.00%)	0 / 245 (0.00%)	1 / 235 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatic mass			
subjects affected / exposed	0 / 243 (0.00%)	0 / 245 (0.00%)	1 / 235 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 243 (0.41%)	0 / 245 (0.00%)	0 / 235 (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
Reproductive system and breast disorders			
Cervical dysplasia			

subjects affected / exposed	1 / 243 (0.41%)	0 / 245 (0.00%)	0 / 235 (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
Prostatitis			
subjects affected / exposed	0 / 243 (0.00%)	0 / 245 (0.00%)	1 / 235 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Bipolar I disorder			
subjects affected / exposed	1 / 243 (0.41%)	0 / 245 (0.00%)	0 / 235 (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
Homicidal ideation			
subjects affected / exposed	1 / 243 (0.41%)	0 / 245 (0.00%)	0 / 235 (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
Suicidal ideation			
subjects affected / exposed	1 / 243 (0.41%)	0 / 245 (0.00%)	0 / 235 (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
Renal and urinary disorders			
Calculus bladder			
subjects affected / exposed	1 / 243 (0.41%)	0 / 245 (0.00%)	0 / 235 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 243 (0.00%)	0 / 245 (0.00%)	1 / 235 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	1 / 243 (0.41%)	0 / 245 (0.00%)	0 / 235 (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

Infections and infestations			
Herpes zoster			
subjects affected / exposed	0 / 243 (0.00%)	1 / 245 (0.41%)	0 / 235 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	0 / 243 (0.00%)	0 / 245 (0.00%)	1 / 235 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia necrotising			
subjects affected / exposed	0 / 243 (0.00%)	0 / 245 (0.00%)	0 / 235 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OLE TAF 25 mg From TDF 300 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 237 (2.11%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lipoma			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung squamous cell carcinoma stage II			

subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Testicular neoplasm			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Muscle rupture			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tendon injury			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wrist fracture			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Varicose vein			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Atrial fibrillation			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatic mass			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostatitis			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Bipolar I disorder			

subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Homicidal ideation			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Calculus bladder			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rotator cuff syndrome			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Herpes zoster			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Necrotising fasciitis			
subjects affected / exposed	0 / 237 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pneumonia necrotising			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	TAF 25 mg	TDF 300 mg	OLE TAF 25 mg From TAF 25 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 243 (12.76%)	28 / 245 (11.43%)	15 / 235 (6.38%)
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	18 / 243 (7.41%)	16 / 245 (6.53%)	11 / 235 (4.68%)
occurrences (all)	23	23	15
Nasopharyngitis			
subjects affected / exposed	13 / 243 (5.35%)	12 / 245 (4.90%)	4 / 235 (1.70%)
occurrences (all)	16	14	4

Non-serious adverse events	OLE TAF 25 mg From TDF 300 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 237 (6.33%)		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	12 / 237 (5.06%)		
occurrences (all)	15		
Nasopharyngitis			
subjects affected / exposed	3 / 237 (1.27%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 December 2016	• Tenofovir alafenamide (TAF) had been approved by US Food and Drug administration on 10 November 2016 and is now referred to as Vemlidy®. • Characterization of hepatic status, particularly for subjects with compensated cirrhosis, by Child-Pugh score added to protocol assessments. • Primary endpoint changed from Week 24 to Week 48. Statistical analysis of primary endpoint analysis changed from Week 24 to 48. The primary analysis will be performed when last subject had completed Week 48 or discontinued prematurely. • Approximate number of subjects planned changed from 300 to 460 subjects. • Primary and Secondary efficacy endpoints changed from Week 24 to 48. Secondary safety endpoints changed from Week 24 to Week 48. • Updated the use of anticonvulsants from use with caution to prohibited during the study in order to align with the US prescribing information for Vemlidy. • The non-inferiority margin was changed from 6% to 4%. • The power of primary endpoint and key secondary safety endpoints were updated based on the new non-inferiority margin and new time point had changed from Week 24 to Week 48.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32087795