Clinical trial results:
A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of Tenofovir Alafenamide (TAF) 25 mg QD versus Tenofovir Disoproxil Fumarate (TDF) 300 mg QD for the Treatment of HBeAg-Negative, Chronic Hepatitis B

Summary

EudraCT number	2013-000626-63
Trial protocol	IT GB DE ES PL
Global end of trial date	

Results information

Result version number	v1
This version publication date	21 September 2023
First version publication date	21 September 2023

Trial information

Trial identification

Sponsor protocol code	GS-US-320-0108

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01940341
WHO universal trial number (UTN)	-
Other trial identifiers	NCT02836236: ClinicalTrials.gov identifier (NCT number)

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	Interim
Date of interim/final analysis	31 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 September 2015
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to compare the efficacy, safety, and tolerability of tenofovir alafenamide (TAF) versus tenofovir disoproxil fumarate (TDF) in treatment-naive and treatment-experienced adults with hepatitis B e antigen (HBeAg)-negative chronic hepatitis B virus (HBV) infection. Results presented include Week 384 final data for the main study (Global cohorts) and Week 48 interim data for China study.

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:

This study was conducted globally in multiple countries including China. As enrollment began later on clinicaltrials.gov, it has separately registered. Global study has NCT identifier - NCT01940341 and China study has identifier - NCT02836236.

Evidence for comparator: -

Actual start date of recruitment	12 September 2013
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	China: 155
Country: Number of subjects enrolled	Hong Kong: 69
Country: Number of subjects enrolled	Canada: 46
Country: Number of subjects enrolled	Korea, Republic of: 46
Country: Number of subjects enrolled	Taiwan: 37
Country: Number of subjects enrolled	United States: 37
Country: Number of subjects enrolled	Russian Federation: 35
Country: Number of subjects enrolled	India: 33
Country: Number of subjects enrolled	Japan: 27
Country: Number of subjects enrolled	Romania: 21
Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	Turkey: 14
Country: Number of subjects enrolled	New Zealand: 12
Country: Number of subjects enrolled	Australia: 10

Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Spain: 3
Worldwide total number of subjects	581
EEA total number of subjects	54

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)	564
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in East Asia, Europe, North America, Australia, India, and New Zealand.

Pre-assignment

Screening details:

877 participants were screened in global cohorts and 239 participants were screened in China cohort.

Period 1

Period 1 title	Double-Blind 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 (Global)

Arm description:

TAF 25 mg tablet + TDF placebo tablet once daily for up to 96 weeks (per amendment 1 & 2) or 144 weeks (per amendment 3).

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

Dosage and administration details:

25 mg administered once daily.

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

Dosage and administration details:

Administered once daily.

Arm title	TDF 300 mg (Global)

Arm description:

TDF 300 mg tablet + TAF placebo tablet once daily for up to 96 weeks (per amendment 1 & 2) or 144 weeks (per amendment 3).

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

Dosage and administration details:

300 mg administered once daily.

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

Dosage and administration details:
Administered once daily.

Arm title	TAF 25 mg (China)

Arm description:
TAF 25 mg tablet + TDF placebo tablet once daily for up to 144 weeks.

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

Dosage and administration details:
25 mg administered once daily.

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

Dosage and administration details:
Administered once daily.

Arm title	TDF 300 mg (China)

Arm description:
TDF 300 mg tablet + TAF placebo tablet once daily for up to 144 weeks.

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

Dosage and administration details:
300 mg administered once daily.

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

Dosage and administration details:
Administered once daily.

Number of subjects in period 1[1]	TAF 25 mg (Global)	TDF 300 mg (Global)	TAF 25 mg (China)
Started	285	140	104
Completed	261	129	0
Not completed	24	11	104
Withdrew Consent	7	4	2
Protocol specified criteria for withdrawal	1	-	-
Death	-	1	-
Adverse event	4	2	-
Non-compliance with study drug	1	1	-
Lost to follow-up	8	1	-
Investigator's discretion	3	1	1
Continuing Study	-	-	101
Pregnancy	-	1	-

Number of subjects in period 1[1]	TDF 300 mg (China)
Started	50
Completed	0
Not completed	50
Withdrew Consent	-
Protocol specified criteria for withdrawal	-
Death	-
Adverse event	1
Non-compliance with study drug	-
Lost to follow-up	-
Investigator's discretion	-
Continuing Study	49
Pregnancy	-

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: Global study - One participant randomised to TDF arm did not receive treatment.
China study - One participant randomised to TAF arm did not receive treatment.

Period 2

Period 2 title	Open-Label TAF Extension Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	TAF 25 mg to TAF 25 mg (Global)

Arm description:

After Week 96 or 144 in the Blinded Treatment Phase, participants were given the option to continue with Open-label (OL) TAF 25 mg for additional 288 or 240 weeks (Up to Week 384), respectively.

After the completion of OL TAF Extension Phase treatment or when there was early discontinuation of treatment, participants either switched to commercially available anti-HBV treatments in their country or entered follow-up phase and were followed-up every 4 weeks for 24 weeks off treatment (treatment-free follow-up [TFFU]) for the assessment of safety.

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

Dosage and administration details:

25 mg administered once daily.

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

Dosage and administration details:

Administered once daily.

Arm title	TDF 300 mg to TAF 25 mg (Global)

Arm description:

After Week 96 or 144 in the Blinded Treatment Phase, participants were given the option to switch to OL TAF 25 mg for additional 288 or 240 weeks (Up to Week 384), respectively.

After the completion of OL TAF Extension Phase treatment or when there was early discontinuation of treatment, participants either switched to commercially available anti-HBV treatments in their country or entered follow-up phase and were followed-up every 4 weeks for 24 weeks off treatment (TFFU) for the assessment of safety.

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

Dosage and administration details:

300 mg administered once daily.

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

Dosage and administration details:

Administered once daily.

Number of subjects in period 2	TAF 25 mg to TAF 25 mg (Global)	TDF 300 mg to TAF 25 mg (Global)
Started	261	129
Completed	227	118
Not completed	34	11
Withdrew Consent	17	4
Lost to follow-up	6	-
Protocol specified criteria for withdrawal	3	1
Death	1	-
Pregnancy	-	1
Adverse event	2	-
Non-compliance with study drug	-	1
Investigator's discretion	3	4
Progressive disease	1	-
Hbsag seroconversion	1	-

Baseline characteristics

Reporting groups	
Reporting group title	TAF 25 mg (Global)
Reporting group description:	
TAF 25 mg tablet + TDF placebo tablet once daily for up to 96 weeks (per amendment 1 & 2) or 144 weeks (per amendment 3).	
Reporting group title	TDF 300 mg (Global)
Reporting group description:	
TDF 300 mg tablet + TAF placebo tablet once daily for up to 96 weeks (per amendment 1 & 2) or 144 weeks (per amendment 3).	
Reporting group title	TAF 25 mg (China)
Reporting group description:	
TAF 25 mg tablet + TDF placebo tablet once daily for up to 144 weeks.	
Reporting group title	TDF 300 mg (China)
Reporting group description:	
TDF 300 mg tablet + TAF placebo tablet once daily for up to 144 weeks.	

Reporting group values	TAF 25 mg (Global)	TDF 300 mg (Global)	TAF 25 mg (China)
Number of subjects	285	140	104
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	276	136	102
>=65 years	9	4	2
Age continuous Units: years			
arithmetic mean	45	48	42
standard deviation	± 11.6	± 10.4	± 9.9
Gender categorical Units: Subjects			
Female	112	54	30
Male	173	86	74
Race Units: Subjects			
Asian	205	102	104
White	71	35	0
Black or African American	5	3	0
Other or More Than One Race	2	0	0
Native Hawaiian or Other Pacific Islander	2	0	0
Ethnicity Units: Subjects			
Not Hispanic or Latino	279	140	104
Unknown or Not Reported	4	0	0
Hispanic or Latino	2	0	0
IL28B Genotype			
The CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	209	106	94

CT	65	23	8
TT	10	9	1
Missing	1	2	1
Plasma HBV DNA Level Units: Subjects			
< 7 log10 IU/mL	230	116	77
>= 7 log10 IU/mL - < 8 log10 IU/mL	42	20	21
>= 8 log10 IU/mL	13	4	6
Oral Antiviral Treatment Status Units: Subjects			
Treatment Experienced	60	31	41
Treatment Naive	225	109	63
Proteinuria by Urinalysis (dipstick) Units: Subjects			
Grade 0	270	135	101
Grade 1	13	5	3
Grade 2	2	0	0
Grade 3	0	0	0
HBV DNA Units: log10 IU/mL			
arithmetic mean	5.7	5.8	5.5
standard deviation	± 1.34	± 1.32	± 1.73

Reporting group values	TDF 300 mg (China)	Total	
Number of subjects	50	579	
Age categorical Units: Subjects			
<=18 years	0	0	
Between 18 and 65 years	48	562	
>=65 years	2	17	
Age continuous Units: years			
arithmetic mean	45		
standard deviation	± 11.2	-	
Gender categorical Units: Subjects			
Female	12	208	
Male	38	371	
Race Units: Subjects			
Asian	50	461	
White	0	106	
Black or African American	0	8	
Other or More Than One Race	0	2	
Native Hawaiian or Other Pacific Islander	0	2	
Ethnicity Units: Subjects			
Not Hispanic or Latino	50	573	
Unknown or Not Reported	0	4	
Hispanic or Latino	0	2	

IL28B Genotype			
The CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	39	448	
CT	10	106	
TT	1	21	
Missing	0	4	
Plasma HBV DNA Level Units: Subjects			
< 7 log10 IU/mL	39	462	
>= 7 log10 IU/mL - < 8 log10 IU/mL	10	93	
>= 8 log10 IU/mL	1	24	
Oral Antiviral Treatment Status Units: Subjects			
Treatment Experienced	20	152	
Treatment Naive	30	427	
Proteinuria by Urinalysis (dipstick) Units: Subjects			
Grade 0	48	554	
Grade 1	2	23	
Grade 2	0	2	
Grade 3	0	0	
HBV DNA Units: log10 IU/mL			
arithmetic mean	5.3		
standard deviation	± 1.63	-	

End points

End points reporting groups

Reporting group title	TAF 25 mg (Global)
Reporting group description:	
TAF 25 mg tablet + TDF placebo tablet once daily for up to 96 weeks (per amendment 1 & 2) or 144 weeks (per amendment 3).	
Reporting group title	TDF 300 mg (Global)
Reporting group description:	
TDF 300 mg tablet + TAF placebo tablet once daily for up to 96 weeks (per amendment 1 & 2) or 144 weeks (per amendment 3).	
Reporting group title	TAF 25 mg (China)
Reporting group description:	
TAF 25 mg tablet + TDF placebo tablet once daily for up to 144 weeks.	
Reporting group title	TDF 300 mg (China)
Reporting group description:	
TDF 300 mg tablet + TAF placebo tablet once daily for up to 144 weeks.	
Reporting group title	TAF 25 mg to TAF 25 mg (Global)
Reporting group description:	
After Week 96 or 144 in the Blinded Treatment Phase, participants were given the option to continue with Open-label (OL) TAF 25 mg for additional 288 or 240 weeks (Up to Week 384), respectively. After the completion of OL TAF Extension Phase treatment or when there was early discontinuation of treatment, participants either switched to commercially available anti-HBV treatments in their country or entered follow-up phase and were followed-up every 4 weeks for 24 weeks off treatment (treatment-free follow-up [TFFU]) for the assessment of safety.	
Reporting group title	TDF 300 mg to TAF 25 mg (Global)
Reporting group description:	
After Week 96 or 144 in the Blinded Treatment Phase, participants were given the option to switch to OL TAF 25 mg for additional 288 or 240 weeks (Up to Week 384), respectively. After the completion of OL TAF Extension Phase treatment or when there was early discontinuation of treatment, participants either switched to commercially available anti-HBV treatments in their country or entered follow-up phase and were followed-up every 4 weeks for 24 weeks off treatment (TFFU) for the assessment of safety.	

Primary: Percentage of Participants with Hepatitis B Virus (HBV) DNA < 29 IU/mL (Missing = Failure)

End point title	Percentage of Participants with Hepatitis B Virus (HBV) DNA < 29 IU/mL (Missing = Failure)
End point description:	
Full Analysis Set included participants who were randomized into the study and received at least 1 dose of study drugs. Participants were analyzed according to the treatment to which they were randomized. A Missing = Failure approach was employed for the efficacy endpoints, in which all missing data will be treated as not achieving the endpoint.	
End point type	Primary
End point timeframe:	
Week 48	

End point values	TAF 25 mg (Global)	TDF 300 mg (Global)	TAF 25 mg (China)	TDF 300 mg (China)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	285	140	104	50
Units: Percentage of Participants				
number (not applicable)	94.0	92.9	89.4	98.0

Statistical analyses

Statistical analysis title	Participants with HBV DNA < 29 IU/mL at Week 48

Statistical analysis description:

The null hypothesis was that the TAF group is at least 10% worse than the TDF group with respect to the proportion of participants with HBV DNA < 29 IU/mL at Week 48. The alternative hypothesis was that the TAF group is less than 10% worse than the TDF group with respect to the proportion of participants with HBV DNA < 29 IU/mL at Week 48. Noninferiority was assessed using a 95% CI, with a noninferiority margin of 10%. Data adjusted by baseline HBV DNA categories+oral antiviral treatment status.

Comparison groups	TAF 25 mg (Global) v TDF 300 mg (Global)
Number of subjects included in analysis	425
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in percentage of partcipants
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	7.2

Notes:

[1] - Sample sizes of 130 and 260 participants in the TDF and TAF groups, respectively, were planned to give 84% power to rule out the noninferiority margin of 10% at a 1-sided significance level of 0.025. This sample size based on the assumption that expected difference (TAF−TDF) in proportion of participants with HBV DNA < 29 IU/mL was 0 and the proportion of participants with HBV DNA < 29 IU/mL in TDF group=69%. Missing data=not achieving the primary endpoint.

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:

Participants in the Hip Dual-Energy X-ray Absorptiometry (DXA) Analysis Set (participants who were randomized, received at least 1 dose of study drugs, and had nonmissing baseline hip BMD values) with available data were analyzed. Participants were analyzed according to the treatment they actually received. Missing data were excluded from analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	TAF 25 mg (Global)	TDF 300 mg (Global)	TAF 25 mg (China)	TDF 300 mg (China)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	270	133	39	22
Units: Percentage change				
arithmetic mean (standard deviation)				
Change at Week 48	-0.288 (± 2.1448)	-2.156 (± 2.1672)	-0.718 (± 2.0131)	-1.096 (± 2.9200)

Statistical analyses

No statistical analyses for this end point

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:

Participants in the Spine DXA Analysis Set (participants who were randomized, received at least 1 dose of study drugs, and had nonmissing baseline spine BMD values) with available data were analyzed. Participants were analyzed according to the treatment they actually received. Missing data were excluded from analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	TAF 25 mg (Global)	TDF 300 mg (Global)	TAF 25 mg (China)	TDF 300 mg (China)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	271	133	39	22
Units: Percentage change				
arithmetic mean (standard deviation)				
Change at Week 48	-0.876 (± 2.8558)	-2.514 (± 3.3558)	0.740 (± 3.3764)	-3.456 (± 3.1071)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Serum Creatinine at Week 48

End point title	Change From Baseline in Serum Creatinine at Week 48

End point description:

Participants in the Safety Analysis Set (participants who were randomized into the study and received at least 1 dose of study drug) with available data were analyzed. Participants were analyzed according to the treatment they actually received.
Missing data were excluded from analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 48

End point values	TAF 25 mg (Global)	TDF 300 mg (Global)	TAF 25 mg (China)	TDF 300 mg (China)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	275	135	101	49
Units: Percentage change				
arithmetic mean (standard deviation)				
Change at Week 48	0.01 (± 0.092)	0.02 (± 0.103)	0.012 (± 0.0827)	0.030 (± 0.0754)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants With Treatment-emergent Proteinuria by Urinalysis (Dipstick) Through Week 48

End point title	Percentage of Participants With Treatment-emergent Proteinuria by Urinalysis (Dipstick) Through Week 48

End point description:

Grades 1 (mild), 2 (moderate), and 3 (severe) were the highest treatment-emergent postbaseline grades for urine protein using the dipstick method. Participants in the Safety Analysis Set with at least 1 postbaseline urine protein value were analyzed.

End point type	Other pre-specified

End point timeframe:

Up to 48 weeks

End point values	TAF 25 mg (Global)	TDF 300 mg (Global)	TAF 25 mg (China)	TDF 300 mg (China)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	282	140	102	50
Units: Percentage of participants				
number (not applicable)				
Grade 1	18.1	16.4	21.6	18.0
Grade 2	1.1	2.1	2.9	4.0
Grade 3	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Deaths: For Global cohorts: Randomization up to approximately 427.6 weeks. For China Cohort: Up to Week 48 Data cut; Adverse events - For Global cohorts: First dose date up to Week 384. For China Cohort: Up to Week 48 Data cut

Adverse event reporting additional description:

All-cause mortality: Randomized Analysis Set: All participants randomized into the study. Adverse events: Safety Analysis Set: Participants who received at least 1 dose of study drug in the respective period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	TAF 25 mg (Global)

Reporting group description:

TAF 25 mg tablet + TDF placebo tablet once daily for up to 96 weeks (per amendment 1 & 2) or 144 weeks (per amendment 3).

Reporting group title	TDF 300 mg (Global)

Reporting group description:

TDF 300 mg tablet + TAF placebo tablet once daily for up to 96 weeks (per amendment 1 & 2) or 144 weeks (per amendment 3).

Reporting group title	TAF 25 mg to TAF 25 mg (Global)

Reporting group description:

After Week 144 in the Blinded Treatment Phase, participants were given the option to continue with OL TAF for additional 288 or 240 weeks (Up to Week 384).

After the end of treatment in OL phase or Blinded Treatment Phase, participants either switched to commercially available anti-HBV treatments in their country or entered follow-up phase and were followed-up every 4 weeks for 24 weeks for the assessment of safety.

Reporting group title	TDF 300 mg (China)

Reporting group description:

TAF 25 mg tablet + TDF placebo tablet once daily for up to 144 weeks.

Reporting group title	TDF 300 mg to TAF 25 mg (Global)

Reporting group description:

After Week 144 in the Blinded Treatment Phase, participants were given the option to switch to Open-label (OL) TAF for additional 288 or 240 weeks (Up to Week 384).

After the end of treatment in OL phase or Blinded Treatment Phase, participants either switched to commercially available anti-HBV treatments in their country or entered follow-up phase and were followed-up every 4 weeks for 24 weeks for the assessment of safety.

Reporting group title	TAF 25 mg (China)

Reporting group description:

TAF 25 mg tablet + TAF placebo tablet once daily for up to 144 weeks

Serious adverse events	TAF 25 mg (Global)	TDF 300 mg (Global)	TAF 25 mg to TAF 25 mg (Global)
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 285 (9.12%)	17 / 140 (12.14%)	17 / 129 (13.18%)
number of deaths (all causes)	0	2	1

number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	2 / 285 (0.70%)	4 / 140 (2.86%)	3 / 129 (2.33%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	2 / 285 (0.70%)	0 / 140 (0.00%)	0 / 129 (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
Adenocarcinoma of colon			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Breast cancer in situ			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Breast cancer stage I			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Lung neoplasm malignant			

subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Metastases to lung			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Pancreatic carcinoma metastatic			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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			
Hypertension			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Pyrexia			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 285 (0.00%)	1 / 140 (0.71%)	0 / 129 (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
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Confusional state			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Device breakage			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Investigations			
Lymphocyte count increased			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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			

Head injury			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Clavicle fracture			
subjects affected / exposed	0 / 285 (0.00%)	1 / 140 (0.71%)	0 / 129 (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
Foot fracture			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Foreign body			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Hand fracture			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Heat exhaustion			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Hip fracture			
subjects affected / exposed	0 / 285 (0.00%)	1 / 140 (0.71%)	0 / 129 (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
Joint injury			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Meniscus injury			

subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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 rupture			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Skin laceration			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural complication			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Pelvic fracture			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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 disorders			
Coronary artery disease			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 285 (0.00%)	1 / 140 (0.71%)	0 / 129 (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
Cardiopulmonary failure			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Palpitations			

subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Nervous system disorders			
Bell's palsy			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical radiculopathy			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 285 (0.00%)	1 / 140 (0.71%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			

subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Presyncope			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Syncope			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	2 / 129 (1.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Gastritis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Abdominal pain			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			

subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Inguinal hernia			
subjects affected / exposed	0 / 285 (0.00%)	1 / 140 (0.71%)	0 / 129 (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
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 285 (0.00%)	1 / 140 (0.71%)	0 / 129 (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
Enteritis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Colitis ulcerative			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Toothache			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Rectal polyp			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Obstructive pancreatitis			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Large intestine polyp			

subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stenosis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Cholecystitis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Cholelithiasis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Hepatic fibrosis			
subjects affected / exposed	0 / 285 (0.00%)	1 / 140 (0.71%)	0 / 129 (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
Cholangitis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Renal and urinary disorders			

Calculus urinary			
subjects affected / exposed	0 / 285 (0.00%)	2 / 140 (1.43%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	2 / 285 (0.70%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Haematuria			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Hydronephrosis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Renal colic			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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 impairment			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Urinary retention			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Musculoskeletal and connective tissue disorders			

Lumbar spinal stenosis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Arthralgia			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 285 (0.00%)	1 / 140 (0.71%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Spinal osteoarthritis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Spondylolisthesis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Pneumonia			
subjects affected / exposed	1 / 285 (0.35%)	1 / 140 (0.71%)	2 / 129 (1.55%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cellulitis			
subjects affected / exposed	0 / 285 (0.00%)	2 / 140 (1.43%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 285 (0.00%)	1 / 140 (0.71%)	0 / 129 (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
Appendicitis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Upper respiratory tract infection			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Chronic hepatitis B			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Gastroenteritis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	0 / 129 (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
Escherichia urinary tract infection			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Escherichia bacteraemia			

subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Otitis externa			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasmodium vivax infection			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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
Urinary tract infection			
subjects affected / exposed	0 / 285 (0.00%)	1 / 140 (0.71%)	0 / 129 (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
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 285 (0.35%)	1 / 140 (0.71%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	1 / 285 (0.35%)	0 / 140 (0.00%)	0 / 129 (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

Serious adverse events	TDF 300 mg (China)	TDF 300 mg to TAF 25 mg (Global)	TAF 25 mg (China)
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 50 (10.00%)	38 / 261 (14.56%)	5 / 104 (4.81%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			

subjects affected / exposed	0 / 50 (0.00%)	6 / 261 (2.30%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Adenocarcinoma of colon			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Breast cancer in situ			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Breast cancer stage I			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 261 (0.00%)	0 / 104 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Lung neoplasm malignant			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Malignant melanoma			

subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Metastases to lung			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Pyrexia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Chest pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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			
Drug hypersensitivity			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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

Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Confusional state			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Device breakage			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Investigations			
Lymphocyte count increased			
subjects affected / exposed	1 / 50 (2.00%)	0 / 261 (0.00%)	0 / 104 (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
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Clavicle fracture			

subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Foot fracture			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Foreign body			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Hand fracture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Heat exhaustion			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Hip fracture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Joint injury			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Meniscus injury			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Tendon rupture			

subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Post procedural complication			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Pelvic fracture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	0 / 50 (0.00%)	2 / 261 (0.77%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Cardiopulmonary failure			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Palpitations			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Sinus node dysfunction			

subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Bell's palsy			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Cervical radiculopathy			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Carpal tunnel syndrome			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Dizziness			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Presyncope			

subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Syncope			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 50 (0.00%)	2 / 261 (0.77%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 50 (0.00%)	2 / 261 (0.77%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Ascites			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Inguinal hernia			

subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Enteritis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Toothache			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Rectal polyp			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Obstructive pancreatitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Large intestine polyp			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Hepatobiliary disorders			
Cholecystitis acute			

subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Bile duct stenosis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Cholecystitis			
subjects affected / exposed	1 / 50 (2.00%)	1 / 261 (0.38%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 50 (2.00%)	2 / 261 (0.77%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic fibrosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Cholangitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Hepatic function abnormal			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Ureterolithiasis			

subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Nephrolithiasis			
subjects affected / exposed	0 / 50 (0.00%)	2 / 261 (0.77%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Hydronephrosis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Renal colic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Renal impairment			
subjects affected / exposed	1 / 50 (2.00%)	0 / 261 (0.00%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Back pain			

subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Arthralgia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Osteoarthritis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Spinal osteoarthritis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Spinal stenosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Spondylolisthesis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Cellulitis			

subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Pyelonephritis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Appendicitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 261 (0.00%)	0 / 104 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Chronic hepatitis B			
subjects affected / exposed	1 / 50 (2.00%)	0 / 261 (0.00%)	0 / 104 (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
Gastroenteritis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Escherichia urinary tract infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Escherichia bacteraemia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Otitis externa			

subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Plasmodium vivax infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Urinary tract infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 261 (0.38%)	0 / 104 (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
Gout			
subjects affected / exposed	0 / 50 (0.00%)	0 / 261 (0.00%)	0 / 104 (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

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

Non-serious adverse events	TAF 25 mg (Global)	TDF 300 mg (Global)	TAF 25 mg to TAF 25 mg (Global)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	185 / 285 (64.91%)	92 / 140 (65.71%)	58 / 129 (44.96%)
Investigations			
Blood parathyroid hormone increased			
subjects affected / exposed	1 / 285 (0.35%)	1 / 140 (0.71%)	0 / 129 (0.00%)
occurrences (all)	1	1	0
Weight decreased			
subjects affected / exposed	2 / 285 (0.70%)	2 / 140 (1.43%)	0 / 129 (0.00%)
occurrences (all)	2	2	0
Vascular disorders			

Hypertension			
subjects affected / exposed	8 / 285 (2.81%)	9 / 140 (6.43%)	11 / 129 (8.53%)
occurrences (all)	10	9	12
Nervous system disorders			
Dizziness			
subjects affected / exposed	8 / 285 (2.81%)	7 / 140 (5.00%)	4 / 129 (3.10%)
occurrences (all)	9	8	7
Headache			
subjects affected / exposed	53 / 285 (18.60%)	15 / 140 (10.71%)	10 / 129 (7.75%)
occurrences (all)	118	42	21
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	17 / 285 (5.96%)	10 / 140 (7.14%)	4 / 129 (3.10%)
occurrences (all)	18	12	4
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	13 / 285 (4.56%)	3 / 140 (2.14%)	3 / 129 (2.33%)
occurrences (all)	18	6	3
Diarrhoea			
subjects affected / exposed	17 / 285 (5.96%)	5 / 140 (3.57%)	7 / 129 (5.43%)
occurrences (all)	18	5	8
Nausea			
subjects affected / exposed	18 / 285 (6.32%)	10 / 140 (7.14%)	1 / 129 (0.78%)
occurrences (all)	20	10	1
Abdominal distension			
subjects affected / exposed	7 / 285 (2.46%)	1 / 140 (0.71%)	3 / 129 (2.33%)
occurrences (all)	7	1	3
Toothache			
subjects affected / exposed	9 / 285 (3.16%)	3 / 140 (2.14%)	2 / 129 (1.55%)
occurrences (all)	9	3	2
Chronic gastritis			
subjects affected / exposed	0 / 285 (0.00%)	0 / 140 (0.00%)	1 / 129 (0.78%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	11 / 285 (3.86%)	8 / 140 (5.71%)	3 / 129 (2.33%)
occurrences (all)	15	9	3

Abdominal pain			
subjects affected / exposed	15 / 285 (5.26%)	3 / 140 (2.14%)	3 / 129 (2.33%)
occurrences (all)	19	3	3
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 285 (1.05%)	3 / 140 (2.14%)	2 / 129 (1.55%)
occurrences (all)	3	3	2
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	12 / 285 (4.21%)	1 / 140 (0.71%)	4 / 129 (3.10%)
occurrences (all)	16	1	4
Cough			
subjects affected / exposed	25 / 285 (8.77%)	12 / 140 (8.57%)	8 / 129 (6.20%)
occurrences (all)	34	14	11
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	19 / 285 (6.67%)	7 / 140 (5.00%)	10 / 129 (7.75%)
occurrences (all)	21	8	11
Arthralgia			
subjects affected / exposed	30 / 285 (10.53%)	17 / 140 (12.14%)	8 / 129 (6.20%)
occurrences (all)	35	21	8
Pain in extremity			
subjects affected / exposed	13 / 285 (4.56%)	7 / 140 (5.00%)	3 / 129 (2.33%)
occurrences (all)	14	7	3
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	40 / 285 (14.04%)	19 / 140 (13.57%)	10 / 129 (7.75%)
occurrences (all)	80	27	15
Upper respiratory tract infection			
subjects affected / exposed	38 / 285 (13.33%)	16 / 140 (11.43%)	10 / 129 (7.75%)
occurrences (all)	84	33	39
Influenza			
subjects affected / exposed	18 / 285 (6.32%)	9 / 140 (6.43%)	1 / 129 (0.78%)
occurrences (all)	22	10	1
Pharyngitis			
subjects affected / exposed	12 / 285 (4.21%)	4 / 140 (2.86%)	4 / 129 (3.10%)
occurrences (all)	13	4	4

Urinary tract infection			
subjects affected / exposed	9 / 285 (3.16%)	8 / 140 (5.71%)	6 / 129 (4.65%)
occurrences (all)	12	11	9
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 285 (0.35%)	5 / 140 (3.57%)	0 / 129 (0.00%)
occurrences (all)	1	6	0

Non-serious adverse events	TDF 300 mg (China)	TDF 300 mg to TAF 25 mg (Global)	TAF 25 mg (China)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 50 (66.00%)	114 / 261 (43.68%)	62 / 104 (59.62%)
Investigations			
Blood parathyroid hormone increased			
subjects affected / exposed	4 / 50 (8.00%)	0 / 261 (0.00%)	2 / 104 (1.92%)
occurrences (all)	7	0	3
Weight decreased			
subjects affected / exposed	3 / 50 (6.00%)	0 / 261 (0.00%)	2 / 104 (1.92%)
occurrences (all)	3	0	2
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 50 (2.00%)	15 / 261 (5.75%)	2 / 104 (1.92%)
occurrences (all)	1	15	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 50 (2.00%)	10 / 261 (3.83%)	1 / 104 (0.96%)
occurrences (all)	1	11	1
Headache			
subjects affected / exposed	1 / 50 (2.00%)	27 / 261 (10.34%)	5 / 104 (4.81%)
occurrences (all)	1	56	5
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 50 (2.00%)	5 / 261 (1.92%)	2 / 104 (1.92%)
occurrences (all)	1	5	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	3 / 50 (6.00%)	10 / 261 (3.83%)	7 / 104 (6.73%)
occurrences (all)	3	10	7

Diarrhoea			
subjects affected / exposed	3 / 50 (6.00%)	11 / 261 (4.21%)	4 / 104 (3.85%)
occurrences (all)	3	11	4
Nausea			
subjects affected / exposed	3 / 50 (6.00%)	5 / 261 (1.92%)	1 / 104 (0.96%)
occurrences (all)	3	5	1
Abdominal distension			
subjects affected / exposed	3 / 50 (6.00%)	5 / 261 (1.92%)	4 / 104 (3.85%)
occurrences (all)	3	5	4
Toothache			
subjects affected / exposed	4 / 50 (8.00%)	2 / 261 (0.77%)	2 / 104 (1.92%)
occurrences (all)	5	3	2
Chronic gastritis			
subjects affected / exposed	3 / 50 (6.00%)	3 / 261 (1.15%)	0 / 104 (0.00%)
occurrences (all)	3	3	0
Dyspepsia			
subjects affected / exposed	0 / 50 (0.00%)	9 / 261 (3.45%)	0 / 104 (0.00%)
occurrences (all)	0	12	0
Abdominal pain			
subjects affected / exposed	1 / 50 (2.00%)	9 / 261 (3.45%)	0 / 104 (0.00%)
occurrences (all)	1	9	0
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 50 (4.00%)	15 / 261 (5.75%)	1 / 104 (0.96%)
occurrences (all)	2	15	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 50 (4.00%)	0 / 261 (0.00%)	7 / 104 (6.73%)
occurrences (all)	2	0	7
Cough			
subjects affected / exposed	1 / 50 (2.00%)	13 / 261 (4.98%)	9 / 104 (8.65%)
occurrences (all)	1	14	11
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 50 (0.00%)	13 / 261 (4.98%)	3 / 104 (2.88%)
occurrences (all)	0	14	3
Arthralgia			

subjects affected / exposed	1 / 50 (2.00%)	16 / 261 (6.13%)	3 / 104 (2.88%)
occurrences (all)	1	19	3
Pain in extremity			
subjects affected / exposed	1 / 50 (2.00%)	9 / 261 (3.45%)	2 / 104 (1.92%)
occurrences (all)	1	10	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 50 (12.00%)	19 / 261 (7.28%)	19 / 104 (18.27%)
occurrences (all)	7	35	23
Upper respiratory tract infection			
subjects affected / exposed	5 / 50 (10.00%)	23 / 261 (8.81%)	17 / 104 (16.35%)
occurrences (all)	5	68	18
Influenza			
subjects affected / exposed	4 / 50 (8.00%)	13 / 261 (4.98%)	4 / 104 (3.85%)
occurrences (all)	4	14	5
Pharyngitis			
subjects affected / exposed	2 / 50 (4.00%)	14 / 261 (5.36%)	3 / 104 (2.88%)
occurrences (all)	2	17	3
Urinary tract infection			
subjects affected / exposed	0 / 50 (0.00%)	9 / 261 (3.45%)	1 / 104 (0.96%)
occurrences (all)	0	10	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 50 (6.00%)	0 / 261 (0.00%)	1 / 104 (0.96%)
occurrences (all)	3	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 July 2013	• Extended the double-blind phase from 48 to 96 weeks and added Week 96 evaluations to other secondary objectives, as applicable • Changed the primary efficacy endpoint of proportion of subjects with HBV DNA levels at Week 48 from below 69 IU/mL to below 29 IU/mL • Replaced eGFR with serum creatinine as a key secondary safety objective • Extended duration of ophthalmologic substudy to 144 weeks, with additional ophthalmologic assessment at Weeks 72, 96, and 144 • Clarified and revised study entry criteria • Updated statistical section to reflect changes in objectives and to better define analyses of key secondary efficacy and safety endpoints • Revised the number of subjects for PK substudy from 30 subjects to approximately 16 subjects • Added section for Management of Potential Posterior Uveitis Cases and section for Multiplicity Adjustments
04 December 2013	Lowered the entry criteria for estimated glomerular filtration rate (eGFR) from ≥ 60 mL/min to ≥ 50 mL/min • Clarified and revised study entry criteria • Added clarification regarding subjects who elected an evening study drug dosing schedule: such individuals were no longer required to undergo in-clinic dosing and population PK blood draws at the Week 4 and 12 visits • Updated statistical analysis methods for key secondary endpoints to align with the TAF HIV Phase 3 development program • Added cystatin C to the baseline assessments to accommodate the revision to toxicity management for possible nephrotoxicity • Updated information about the drug formulation for TDF, the comparator, to include the formulation used in developing markets • Updated information on the management of potential nephrotoxicity • Added reflex testing for HEV in the event of an ALT elevation
20 February 2015	This protocol change was only applicable for China: • Added the number of subjects to be enrolled in China • Specified that the dual-energy x-ray absorptiometry (DXA) scan procedure at all protocol-specified visits would be performed only at sites that have the capability • Added statement that fracture risk assessment at the baseline visit was intended for sites with DXA capability only • Added hepatitis E virus (HEV) testing as a reflex test for subjects who discontinued study drug and had confirmed ALT elevation • Updated the Gilead Grading Scale for Severity of Adverse Events and Laboratory Abnormalities to reconcile with the scale that was employed in the global program via an administrative letter
05 February 2016	• Extended the blinded period of the study to Week 144 (from Week 96). • Extended the open label period of the study to Week 384 (from Week 144). • Updated the last study visit date of treatment from Week 144/Early Discontinuation (ED) to Week 384/ED. • Added 10 study visits (Week 168, 192, 216, 240, 264, 288, 312, 336, 360, and 384/ED) to be conducted during the additional 5 years of the study. • Revised visit Week numbers to accommodate extension of blinded and open label periods of the study. • Clarified when open label study drug is to be dispensed to participants who rollover to open-label TAF treatment following Amendment 1 or 2, and under Amendment 3. • Clarified visit windows for analysis timepoints (Weeks 48, 96, and 144) to be in alignment with DXA windows. • Added hepatic ultrasound for surveillance of hepatocellular carcinoma every 24 weeks from visit Week 96 to Week 384/ED.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported