



Clinical trial results:

A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Multi-center Study to Evaluate the Safety and Efficacy of GS-9620 in Combination with Tenofovir Disoproxil Fumarate (TDF) for the Treatment of Subjects with Chronic Hepatitis B and Who Are Currently Not on Treatment

Summary

EudraCT number	2015-002017-30
Trial protocol	GB
Global end of trial date	03 May 2019

Results information

Result version number	v1 (current)
This version publication date	17 May 2020
First version publication date	17 May 2020

Trial information

Trial identification

Sponsor protocol code	GS-US-283-1062
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02579382
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	03 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 January 2017
Global end of trial reached?	Yes
Global end of trial date	03 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the safety, tolerability, and efficacy of vesatolimod (formerly GS-9620) in adults with chronic hepatitis B (CHB) infection who were currently not being treated.

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	10 November 2015
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	United Kingdom: 12
Country: Number of subjects enrolled	Korea, Republic of: 51
Country: Number of subjects enrolled	United States: 43
Country: Number of subjects enrolled	Italy: 32
Country: Number of subjects enrolled	Canada: 23
Country: Number of subjects enrolled	Taiwan: 21
Country: Number of subjects enrolled	Hong Kong: 5
Country: Number of subjects enrolled	New Zealand: 5
Worldwide total number of subjects	192
EEA total number of subjects	44

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)	191
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Asia, Europe, New Zealand, and North America. The first participant was screened on 10 November 2015. The last study visit occurred on 03 May 2019.

Pre-assignment

Screening details:

260 participants were screened.

Period 1

Period 1 title	Main Study 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	TDF + Placebo

Arm description:

Main Study Phase: Tenofovir disoproxil fumarate (TDF) 300 mg tablets orally once daily for up to 48 weeks + placebo administered orally once a week (every 7 days) for 12 doses.

Arm type	Experimental
Investigational medicinal product name	TDF
Investigational medicinal product code	
Other name	Viread
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg administered orally once daily

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo administered orally once a week (every 7 days) for 12 doses

Arm title	TDF + Vesatolimod 1 mg
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Arm description:

Main Study Phase: TDF 300 mg tablets orally once daily for up to 48 weeks + vesatolimod 1 mg tablet orally once a week (every 7 days) for 12 doses.

Arm type	Experimental
Investigational medicinal product name	TDF
Investigational medicinal product code	
Other name	Viread
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg administered orally once daily

Investigational medicinal product name	Vesatolimod
Investigational medicinal product code	
Other name	GS-9620
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg orally once a week (every 7 days) for 12 doses

Arm title	TDF + Vesatolimod 2 mg
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Arm description:

Main Study Phase: TDF 300 mg tablets orally once daily for up to 48 weeks + vesatolimod 2 mg tablet orally once a week (every 7 days) for 12 doses.

Arm type	Experimental
Investigational medicinal product name	TDF
Investigational medicinal product code	
Other name	Viread
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg administered orally once daily

Investigational medicinal product name	Vesatolimod
Investigational medicinal product code	
Other name	GS-9620
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

2 mg orally once a week (every 7 days) for 12 doses

Arm title	TDF + Vesatolimod 4 mg
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Arm description:

Main Study Phase: TDF 300 mg tablets orally once daily for up to 48 weeks + vesatolimod 4 mg tablet orally once a week (every 7 days) for 12 doses.

Arm type	Experimental
Investigational medicinal product name	TDF
Investigational medicinal product code	
Other name	Viread
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg administered orally once daily

Investigational medicinal product name	Vesatolimod
Investigational medicinal product code	
Other name	GS-9620
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

4 mg orally once a week (every 7 days) for 12 doses

Number of subjects in period 1	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg
Started	28	53	56
Completed	28	53	54
Not completed	0	0	2
Lost to follow-up	-	-	2
Withdrew consent	-	-	-
Lack of efficacy	-	-	-

Number of subjects in period 1	TDF + Vesatolimod 4 mg
Started	55
Completed	52
Not completed	3
Lost to follow-up	-
Withdrew consent	2
Lack of efficacy	1

Period 2

Period 2 title	Optional Treatment Extension Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	OPEP: TDF Extension from TDF + Placebo

Arm description:

Optional Treatment Extension Phase (OPEP): At Week 48 participants had the option to continue TDF 300 mg tablets orally once daily up to Week 144.

Arm type	Experimental
Investigational medicinal product name	TDF
Investigational medicinal product code	
Other name	Viread
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg administered orally once daily

Arm title	OPEP: TDF Extension from TDF + Vesatolimod 1 mg
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Arm description:

Optional Treatment Extension Phase: At Week 48 participants had the option to continue TDF 300 mg tablets orally once daily up to Week 144.

Arm type	Experimental
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Investigational medicinal product name	TDF
Investigational medicinal product code	
Other name	Viread
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 300 mg administered orally once daily	
Arm title	OTEP: TDF Extension from TDF + Vesatolimod 2 mg

Arm description:

Optional Treatment Extension Phase: At Week 48 participants had the option to continue TDF 300 mg tablets orally once daily up to Week 144.

Arm type	Experimental
Investigational medicinal product name	TDF
Investigational medicinal product code	
Other name	Viread
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 300 mg administered orally once daily	
Arm title	OTEP: TDF Extension from TDF + Vesatolimod 4 mg

Arm description:

Optional Treatment Extension Phase: At Week 48 participants had the option to continue TDF 300 mg tablets orally once daily up to Week 144.

Arm type	Experimental
Investigational medicinal product name	TDF
Investigational medicinal product code	
Other name	Viread
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use
Dosage and administration details: 300 mg administered orally once daily	

Number of subjects in period 2^[1]	OTEP: TDF Extension from TDF + Placebo	OTEP: TDF Extension from TDF + Vesatolimod 1 mg	OTEP: TDF Extension from TDF + Vesatolimod 2 mg
Started	27	51	54
Completed	26	44	50
Not completed	1	7	4
Non-compliance with Study Drug	-	1	-
Pregnancy	-	1	-
Adverse event	-	1	-
Investigator's discretion	1	-	2
Lost to follow-up	-	1	1
Withdrew consent	-	3	1

Number of subjects in period 2^[1]	OTEP: TDF Extension from TDF + Vesatolimod 4 mg
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Started	49
Completed	44
Not completed	5
Non-compliance with Study Drug	-
Pregnancy	-
Adverse event	-
Investigator's discretion	-
Lost to follow-up	1
Withdrew consent	4

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Participants in the following arms completed the Main Study Phase but did not enter the OTEP: TDF Extension From TDF + Placebo: N = 1; TDF Extension From TDF + Vesatolimod 1 mg: N = 2 ; TDF Extension From TDF + Vesatolimod 4 mg: N = 3.

Baseline characteristics

Reporting groups

Reporting group title	TDF + Placebo
Reporting group description:	
Main Study Phase: Tenofovir disoproxil fumarate (TDF) 300 mg tablets orally once daily for up to 48 weeks + placebo administered orally once a week (every 7 days) for 12 doses.	
Reporting group title	TDF + Vesatolimod 1 mg
Reporting group description:	
Main Study Phase: TDF 300 mg tablets orally once daily for up to 48 weeks + vesatolimod 1 mg tablet orally once a week (every 7 days) for 12 doses.	
Reporting group title	TDF + Vesatolimod 2 mg
Reporting group description:	
Main Study Phase: TDF 300 mg tablets orally once daily for up to 48 weeks + vesatolimod 2 mg tablet orally once a week (every 7 days) for 12 doses.	
Reporting group title	TDF + Vesatolimod 4 mg
Reporting group description:	
Main Study Phase: TDF 300 mg tablets orally once daily for up to 48 weeks + vesatolimod 4 mg tablet orally once a week (every 7 days) for 12 doses.	

Reporting group values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg
Number of subjects	28	53	56
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	41	41	44
standard deviation	± 10.4	± 9.6	± 10.3
Gender categorical			
Units: Subjects			
Female	12	21	16
Male	16	32	40
Race			
Units: Subjects			
Asian	22	41	48
White	4	6	5
Black or African American	1	5	3
Native Hawaiian or Pacific Islander	1	0	0
Other	0	1	0
Ethnicity			
Not Permitted = local regulators did not allow collection of race or ethnicity information.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	28	53	56
Not Permitted	0	0	0
Hepatitis B Envelope Antigen (HBeAg) Status			
Units: Subjects			
HBeAg Status- Negative	17	33	33

HBeAg Status- Positive	11	20	23
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Serum Hepatitis B Surface Antigen (HBsAg) (log10 IU/ mL) Units: log10 IU/mL arithmetic mean standard deviation	3.8 ± 0.84	3.7 ± 0.84	3.5 ± 0.88
Hepatitis B Virus (HBV) DNA Units: log10 IU/mL arithmetic mean standard deviation	5.9 ± 2.10	5.9 ± 1.80	5.6 ± 1.85

Reporting group values	TDF + Vesatolimod 4 mg	Total	
Number of subjects	55	192	
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	44 ± 10.3	-	
Gender categorical Units: Subjects			
Female	20	69	
Male	35	123	
Race Units: Subjects			
Asian	44	155	
White	10	25	
Black or African American	0	9	
Native Hawaiian or Pacific Islander	1	2	
Other	0	1	
Ethnicity			
Not Permitted = local regulators did not allow collection of race or ethnicity information.			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	55	192	
Not Permitted	0	0	
Hepatitis B Envelope Antigen (HBeAg) Status Units: Subjects			
HBeAg Status- Negative	34	117	
HBeAg Status- Positive	21	75	
Serum Hepatitis B Surface Antigen (HBsAg) (log10 IU/ mL) Units: log10 IU/mL arithmetic mean standard deviation	3.6 ± 0.74	-	
Hepatitis B Virus (HBV) DNA Units: log10 IU/mL arithmetic mean	5.9		

standard deviation	± 1.70	-	
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End points

End points reporting groups

Reporting group title	TDF + Placebo
Reporting group description: Main Study Phase: Tenofovir disoproxil fumarate (TDF) 300 mg tablets orally once daily for up to 48 weeks + placebo administered orally once a week (every 7 days) for 12 doses.	
Reporting group title	TDF + Vesatolimod 1 mg
Reporting group description: Main Study Phase: TDF 300 mg tablets orally once daily for up to 48 weeks + vesatolimod 1 mg tablet orally once a week (every 7 days) for 12 doses.	
Reporting group title	TDF + Vesatolimod 2 mg
Reporting group description: Main Study Phase: TDF 300 mg tablets orally once daily for up to 48 weeks + vesatolimod 2 mg tablet orally once a week (every 7 days) for 12 doses.	
Reporting group title	TDF + Vesatolimod 4 mg
Reporting group description: Main Study Phase: TDF 300 mg tablets orally once daily for up to 48 weeks + vesatolimod 4 mg tablet orally once a week (every 7 days) for 12 doses.	
Reporting group title	OTEP: TDF Extension from TDF + Placebo
Reporting group description: Optional Treatment Extension Phase (OTEP): At Week 48 participants had the option to continue TDF 300 mg tablets orally once daily up to Week 144.	
Reporting group title	OTEP: TDF Extension from TDF + Vesatolimod 1 mg
Reporting group description: Optional Treatment Extension Phase: At Week 48 participants had the option to continue TDF 300 mg tablets orally once daily up to Week 144.	
Reporting group title	OTEP: TDF Extension from TDF + Vesatolimod 2 mg
Reporting group description: Optional Treatment Extension Phase: At Week 48 participants had the option to continue TDF 300 mg tablets orally once daily up to Week 144.	
Reporting group title	OTEP: TDF Extension from TDF + Vesatolimod 4 mg
Reporting group description: Optional Treatment Extension Phase: At Week 48 participants had the option to continue TDF 300 mg tablets orally once daily up to Week 144.	

Primary: Mean Change (Measured in log₁₀ IU/mL) in Hepatitis B Surface Antigen (HBsAg) from Baseline at Week 24

End point title	Mean Change (Measured in log ₁₀ IU/mL) in Hepatitis B Surface Antigen (HBsAg) from Baseline at Week 24
End point description: The change from baseline to Week 24 in HBsAg (log ₁₀ IU/mL) was analysed using a mixed model for repeated measures (MMRM). The model included treatment, baseline HBsAg (log ₁₀ IU/mL), baseline Hepatitis B Envelope Antigen (HBeAg) status (positive or negative), baseline alanine aminotransferase (ALT) level relative to upper limit of normal (ULN) (> 19 vs ≤ 19 IU/L for females; > 30 vs ≤ 30 IU/L for males), visit and treatment-by-visit interaction as fixed effects, and visit as a repeated measure. The Full Analysis Set included all participants who were randomised and took at least 1 dose of study drug.	
End point type	Primary
End point timeframe: Baseline; Week 24	

End point values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	53	54	54
Units: IU/mL				
least squares mean (confidence interval 95%)	-0.163 (-0.305 to -0.022)	-0.056 (-0.159 to 0.047)	-0.146 (-0.246 to -0.045)	-0.036 (-0.138 to 0.065)

Statistical analyses

Statistical analysis title	TDF + Vesatolimod 1 mg vs TDF + Placebo
Comparison groups	TDF + Placebo v TDF + Vesatolimod 1 mg
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.227 ^[1]
Method	MMRM
Parameter estimate	Least Squares Mean Difference
Point estimate	0.107
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.067
upper limit	0.282

Notes:

[1] - MMRM model included treatment, baseline ALT level, HBeAg baseline status, baseline HBsAg, visit and treatment-by-visit interaction as fixed effect and visit as repeated measurement.

Statistical analysis title	TDF + Vesatolimod 2 mg vs TDF + Placebo
Comparison groups	TDF + Placebo v TDF + Vesatolimod 2 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.84 ^[2]
Method	MMRM
Parameter estimate	Least Squares Mean Difference
Point estimate	0.018
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.156
upper limit	0.191

Notes:

[2] - MMRM model included treatment, baseline ALT level, HBeAg baseline status, baseline HBsAg, visit and treatment-by-visit interaction as fixed effect and visit as repeated measurement.

Statistical analysis title	TDF + Vesatolimod 4 mg vs TDF + Placebo
Comparison groups	TDF + Placebo v TDF + Vesatolimod 4 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.151 ^[3]
Method	MMRM
Parameter estimate	Least Squares Mean Difference
Point estimate	0.127
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.047
upper limit	0.301

Notes:

[3] - MMRM model included treatment, baseline ALT level, HBeAg baseline status, baseline HBsAg, visit and treatment-by-visit interaction as fixed effect and visit as repeated measurement.

Secondary: Percentage of Participants With HBeAg Loss and Seroconversion at Week 24

End point title	Percentage of Participants With HBeAg Loss and Seroconversion at Week 24
End point description:	
HBeAg loss was defined as qualitative HBeAg result changing from positive at baseline to negative at any postbaseline visit. HBeAg seroconversion was defined as qualitative Hepatitis B Envelope Antibody (HBeAb) result changing from negative at baseline to positive at any postbaseline visit. The Missing (M) = Failure (F) approach was used for this analysis. Participants in the Full Analysis Set who were HBeAg positive at baseline were analysed.	
End point type	Secondary
End point timeframe:	
Week 24	

End point values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	20	23	21
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 HBeAg Loss and Seroconversion at Week 48

End point title	Percentage of Participants With HBeAg Loss and Seroconversion at Week 48
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End point description:

HBeAg loss was defined as qualitative HBeAg result changing from positive at baseline to negative at any postbaseline visit. HBeAg seroconversion was defined as qualitative HBeAb result changing from negative at baseline to positive at any postbaseline visit. The Missing (M) = Failure (F) approach was used for this analysis. Participants in the Full Analysis Set who were HBeAg positive at baseline were analysed.

End point type	Secondary
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End point timeframe:

Week 48

End point values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	20	23	21
Units: percentage of participants				
number (not applicable)	0	5.0	4.3	4.8

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HBsAg Loss and Seroconversion at Week 24

End point title	Percentage of Participants with HBsAg Loss and Seroconversion at Week 24
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End point description:

HBsAg loss was defined as qualitative HBsAg result changing from positive at baseline to negative at any postbaseline visit. HBsAg seroconversion was defined as qualitative Hepatitis B Surface Antibody (HBsAb) result changing from negative at baseline to positive at any postbaseline visit. The Missing (M) = Failure (F) approach was used for this analysis. Participants in the Full Analysis Set who were HBsAg positive at baseline were analysed.

End point type	Secondary
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End point timeframe:

Week 24

End point values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	53	56	55
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 and Seroconversion at Week 48

End point title	Percentage of Participants with HBsAg Loss and Seroconversion at Week 48
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End point description:

HBsAg loss was defined as qualitative HBsAg result changing from positive at baseline to negative at any postbaseline visit. HBsAg seroconversion was defined as qualitative HBsAb result changing from negative at baseline to positive at any postbaseline visit. The Missing (M) = Failure (F) approach was used for this analysis. Participants in the Full Analysis Set who were HBsAg positive at baseline were analysed.

End point type	Secondary
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End point timeframe:

Week 48

End point values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	53	56	55
Units: percentage of participants				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change (Measured in log₁₀ IU/mL) in HBsAg from Baseline at Week 12

End point title	Mean Change (Measured in log ₁₀ IU/mL) in HBsAg from Baseline at Week 12
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End point description:

Participants in the Full Analysis Set with available data were analysed.

End point type	Secondary
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End point timeframe:

Baseline; Week 12

End point values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	53	55	52
Units: log ₁₀ IU/mL				
arithmetic mean (standard deviation)	-0.087 (±)	-0.041 (±)	-0.138 (±)	-0.020 (±)

0.2199)

0.2283)

0.5247)

0.2668)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change (Measured in log₁₀ IU/mL) in HBsAg from Baseline at Week 48

End point title	Mean Change (Measured in log ₁₀ IU/mL) in HBsAg from Baseline at Week 48
End point description: Participants in the Full Analysis Set with available data were analysed.	
End point type	Secondary
End point timeframe: Baseline; Week 48	

End point values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	53	54	53
Units: log ₁₀ IU/mL				
arithmetic mean (standard deviation)	-0.338 (± 0.8922)	-0.079 (± 0.2912)	-0.197 (± 0.5757)	-0.088 (± 0.3700)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a ≥ 0.5 log₁₀ IU/mL Decline in Serum HBsAg Titers from Baseline at Week 12

End point title	Percentage of Participants with a ≥ 0.5 log ₁₀ IU/mL Decline in Serum HBsAg Titers from Baseline at Week 12
End point description: HBsAg ≥ 0.5 log ₁₀ IU/mL decline was defined as a decline from baseline in log ₁₀ IU/mL serum HBsAg ≥ 0.5 at the Week 12 post-baseline visit. Participants in the Full Analysis Set were analysed. Missing values were considered failures.	
End point type	Secondary
End point timeframe: Baseline to Week 12	

End point values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	53	56	55
Units: percentage of participants				
number (not applicable)	7.1	3.8	10.7	1.8

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a ≥ 0.5 log₁₀ IU/mL Decline in Serum HBsAg Titers from Baseline at Week 24

End point title	Percentage of Participants with a ≥ 0.5 log ₁₀ IU/mL Decline in Serum HBsAg Titers from Baseline at Week 24
End point description: HBsAg ≥ 0.5 log ₁₀ IU/mL decline was defined as a decline from baseline in log ₁₀ IU/mL serum HBsAg ≥ 0.5 at the Week 24 post-baseline visit. Participants in the Full Analysis Set were analysed. Missing values were considered failures.	
End point type	Secondary
End point timeframe: Baseline to Week 24	

End point values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	53	56	55
Units: percentage of participants				
number (not applicable)	10.7	3.8	10.7	3.6

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a ≥ 0.5 log₁₀ IU/mL Decline in Serum HBsAg Titers from Baseline at Week 48

End point title	Percentage of Participants with a ≥ 0.5 log ₁₀ IU/mL Decline in Serum HBsAg Titers from Baseline at Week 48
End point description: HBsAg ≥ 0.5 log ₁₀ IU/mL decline was defined as a decline from baseline in log ₁₀ IU/mL serum HBsAg ≥ 0.5 at the Week 12 post-baseline visit. Participants in the Full Analysis Set were analysed. Missing values were considered failures.	
End point type	Secondary
End point timeframe: Baseline to Week 48	

End point values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	53	56	55
Units: percentage of participants				
number (not applicable)	17.9	5.7	16.1	14.5

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Hepatitis B Virus Deoxyribonucleic Acid (HBV DNA) < Lower Limit of Quantitation (LLOQ) at Week 24

End point title	Percentage of Participants With Hepatitis B Virus Deoxyribonucleic Acid (HBV DNA) < Lower Limit of Quantitation (LLOQ) at Week 24
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End point description:

LLOQ for HBV DNA was defined as 20 IU/mL. The participants with missing information were excluded from the analysis. Participants in the Full Analysis Set were analysed.

End point type	Secondary
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End point timeframe:

Week 24

End point values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	53	56	55
Units: percentage of participants				
number (not applicable)	53.6	58.5	59.3	63.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HBV DNA < LLOQ at Week 48

End point title	Percentage of Participants With HBV DNA < LLOQ at Week 48
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End point description:

LLOQ for HBV DNA was defined as 20 IU/mL. The participants with missing information were excluded from the analysis. Participants in the Full Analysis Set were analysed.

End point type	Secondary
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End point timeframe:

Week 48

End point values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	53	56	55
Units: percentage of participants				
number (not applicable)	64.3	62.3	75.9	75.5

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Virologic Breakthrough

End point title	Percentage of Participants Experiencing Virologic Breakthrough
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End point description:

Virologic breakthrough was defined as confirmed HBV DNA \geq 69 IU/mL after having had HBV DNA < 69 IU/mL or confirmed 1.0 log₁₀ IU/mL or greater increase in HBV DNA from nadir. Confirmation requires 2 consecutive occurrences of elevation in HBV DNA to > 69 IU/mL after having had HBV DNA < 69 IU/mL or 1.0 log₁₀ IU/mL or greater increases in HBV DNA from nadir. Participants in the Full Analysis Set were analysed.

End point type	Secondary
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End point timeframe:

Weeks 24 and 48

End point values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	53	56	55
Units: percentage of participants				
number (not applicable)				
Week 24	0	0	1.8	0
Week 48	0	3.8	1.8	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Sequence Changes From Baseline Within the HBV Polymerase/reverse transcriptase (pol/RT)

End point title	Number of Participants With Sequence Changes From Baseline Within the HBV Polymerase/reverse transcriptase (pol/RT)
End point description: Sequence analysis of the HBV pol/RT was attempted for any participant who had HBV DNA \geq 69 IU/mL at Week 48 or early discontinuation. Results of the alignment of Week 48 and baseline sequence were reported as a change from baseline sequence. Participants in the Full Analysis Set with available data were analysed.	
End point type	Secondary
End point timeframe: Baseline; Week 48	

End point values	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	13	5	7
Units: participants	2	4	2	2

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) Parameter: AUClast of Vesatolimod

End point title	Pharmacokinetic (PK) Parameter: AUClast of Vesatolimod ^[4]
End point description: AUClast is defined as the area under the concentration versus time curve from time zero to the last quantifiable concentration. The PK Substudy Analysis Set included all randomised participants who took at least 1 dose of vesatolimod, participated in the PK substudy, and had at least 1 non-missing steady state PK parameter.	
End point type	Secondary
End point timeframe: Week 11: Predose, 0.5, 1, 2, 4, 6, 8, 10, 12, and 24 hours postdose	

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Pharmacokinetics of study drug Vesatolimod was performed.

End point values	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	4	
Units: hours*picogram/milliliter (h*pg/mL)				
arithmetic mean (standard deviation)	5252.3 (\pm 5756.26)	7170.6 (\pm 4569.83)	28537.2 (\pm 23608.94)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUCinf of Vesatolimod

End point title PK Parameter: AUCinf of Vesatolimod^[5]

End point description:

AUCinf is defined as the concentration of drug extrapolated to infinite time. Participants in the PK Substudy Analysis Set were analysed.

End point type Secondary

End point timeframe:

Week 11: Predose, 0.5, 1, 2, 4, 6, 8, 10, 12, and 24 hours postdose

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Pharmacokinetics of study drug Vesatolimod was performed.

End point values	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	4	
Units: h*pg/mL				
arithmetic mean (standard deviation)	7277.3 (± 6550.71)	10239.0 (± 6243.75)	34534.8 (± 26482.89)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: %AUCexp of Vesatolimod

End point title PK Parameter: %AUCexp of Vesatolimod^[6]

End point description:

%AUCexp is defined as the percentage of AUC extrapolated between AUClast and AUCinf. Participants in the PK Substudy Analysis Set were analysed.

End point type Secondary

End point timeframe:

Week 11: Predose, 0.5, 1, 2, 4, 6, 8, 10, 12, and 24 hours postdose

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Pharmacokinetics of study drug Vesatolimod was performed.

End point values	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	4	
Units: percentage				
arithmetic mean (standard deviation)	31.1 (± 19.70)	28.61 (± 11.42)	19.3 (± 6.15)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Cmax of Vesatolimod

End point title	PK Parameter: Cmax of Vesatolimod ^[7]
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End point description:

Cmax is defined as the maximum concentration of drug. Participants in the PK Substudy Analysis Set were analysed.

End point type	Secondary
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End point timeframe:

Week 11: Predose, 0.5, 1, 2, 4, 6, 8, 10, 12, and 24 hours postdose

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Pharmacokinetics of study drug Vesatolimod was performed.

End point values	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	4	
Units: pg/mL				
arithmetic mean (standard deviation)	667.8 (± 785.44)	850.4 (± 569.75)	4957.5 (± 5035.46)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Clast of Vesatolimod

End point title	PK Parameter: Clast of Vesatolimod ^[8]
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End point description:

Clast is defined as the last observable concentration of drug. Participants in the PK Substudy Analysis Set were analysed.

End point type	Secondary
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End point timeframe:

Week 11: Predose, 0.5, 1, 2, 4, 6, 8, 10, 12, and 24 hours postdose

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Pharmacokinetics of study drug Vesatolimod was performed.

End point values	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	4	
Units: pg/mL				
arithmetic mean (standard deviation)	92.8 (± 73.80)	119.0 (± 74.45)	328.0 (± 165.19)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Tmax of Vesatolimod

End point title	PK Parameter: Tmax of Vesatolimod ^[9]
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End point description:

Tmax is defined as the time (observed time point) of Cmax. Participants in the PK Substudy Analysis Set were analysed.

End point type	Secondary
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End point timeframe:

Week 11: Predose, 0.5, 1, 2, 4, 6, 8, 10, 12, and 24 hours postdose

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Pharmacokinetics of study drug Vesatolimod was performed.

End point values	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	4	
Units: hour (h)				
median (full range (min-max))	1.00 (0.47 to 4.00)	2.00 (2.00 to 4.00)	3.00 (1.00 to 4.00)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Tlast of Vesatolimod

End point title	PK Parameter: Tlast of Vesatolimod ^[10]
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End point description:

Tlast is defined as the time (observed time point) of Clast. Participants in the PK Substudy Analysis Set were analysed.

End point type	Secondary
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End point timeframe:

Week 11: Predose, 0.5, 1, 2, 4, 6, 8, 10, 12, and 24 hours postdose

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Pharmacokinetics of study drug Vesatolimod was performed.

End point values	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	4	
Units: hour				
median (full range (min-max))	24.00 (8.00 to 24.00)	24.00 (24.00 to 24.00)	24.00 (24.00 to 24.00)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: T1/2 of Vesatolimod

End point title	PK Parameter: T1/2 of Vesatolimod ^[11]
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End point description:

T1/2 is defined as the estimate of the terminal elimination half-life of the drug. Participants in the PK Substudy Analysis Set were analysed.

End point type	Secondary
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End point timeframe:

Week 11: Predose, 0.5, 1, 2, 4, 6, 8, 10, 12, and 24 hours postdose

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Pharmacokinetics of study drug Vesatolimod was performed.

End point values	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	4	
Units: hour				
median (full range (min-max))	10.79 (4.57 to 50.08)	14.12 (12.32 to 26.49)	13.32 (8.90 to 14.83)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: CL/F of Vesatolimod

End point title	PK Parameter: CL/F of Vesatolimod ^[12]
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End point description:

CL/F is defined as the apparent oral clearance following administration of the drug. Participants in the PK

Substudy Analysis Set were analysed.

End point type	Secondary
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End point timeframe:

Predose, 0.5, 1, 2, 4, 6, 8, 10, 12, and 24 hours postdose

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Pharmacokinetics of study drug Vesatolimod was performed.

End point values	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg	TDF + Vesatolimod 4 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	4	
Units: liter/hour				
arithmetic mean (standard deviation)	273.9 (± 270.58)	262.3 (± 144.45)	156.2 (± 72.48)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose date up to last dose of study drug (Maximum: 144 weeks)

Adverse event reporting additional description:

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

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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Reporting groups

Reporting group title	TDF + Placebo
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Reporting group description:

Main Study Phase: Placebo administered orally once a week (every 7 days) for 12 doses + tenofovir disoproxil fumarate (TDF) 300 mg tablets orally once daily for up to 48 weeks.

Reporting group title	TDF + Vesatolimod 1 mg
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Reporting group description:

Main Study Phase: Vesatolimod (GS 9620) 1 mg tablet orally once a week (every 7 days) for 12 doses + TDF 300 mg tablets orally once daily for up to 48 weeks.

Reporting group title	TDF + Vesatolimod 2 mg
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Reporting group description:

Main Study Phase: Vesatolimod 2 mg tablet orally once a week (every 7 days) for 12 doses + TDF 300 mg tablets orally once daily for up to 48 weeks.

Reporting group title	TDF + Vesatolimod 4 mg
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Reporting group description:

Main Study Phase: Vesatolimod 4 mg tablet orally once a week (every 7 days) for 12 doses + TDF 300 mg tablets orally once daily for up to 48 weeks.

Reporting group title	TDF Extension From TDF + Placebo
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Reporting group description:

Optional Treatment Extension Phase: At Week 48 participants had the option to continue TDF 300 mg tablets orally once daily up to Week 144; includes participants who received TDF + Placebo in the Main Study Phase.

Reporting group title	TDF Extension From TDF + Vesatolimod 1 mg
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Reporting group description:

Optional Treatment Extension Phase: At Week 48 participants had the option to continue TDF 300 mg tablets orally once daily up to Week 144; includes participants who received TDF + Vesatolimod 1 mg in the Main Study Phase.

Reporting group title	TDF Extension From TDF + Vesatolimod 2 mg
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Reporting group description:

Optional Treatment Extension Phase: At Week 48 participants had the option to continue TDF 300 mg tablets orally once daily up to Week 144; includes participants who received TDF + Vesatolimod 2 mg in the Main Study Phase.

Reporting group title	TDF Extension from TDF + Vesatolimod 4 mg
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Reporting group description:

Optional Treatment Extension Phase: At Week 48 participants had the option to continue TDF 300 mg tablets orally once daily up to Week 144; includes participants who received TDF + Vesatolimod 4 mg in the Main Study Phase.

Serious adverse events	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	1 / 56 (1.79%)
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 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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
Leiomyoma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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			
Skin laceration			
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	0 / 56 (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
Tendon rupture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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			
Facial paralysis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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
Hemiparesis			

subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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 pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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 congestion			

subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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
Uterine haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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
Uterine polyp			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 56 (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			
Asthma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	TDF + Vesatolimod 4 mg	TDF Extension From TDF + Placebo	TDF Extension From TDF + Vesatolimod 1 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 55 (1.82%)	1 / 27 (3.70%)	4 / 51 (7.84%)
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 / 55 (0.00%)	0 / 27 (0.00%)	2 / 51 (3.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 55 (0.00%)	0 / 27 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leiomyoma			

subjects affected / exposed	0 / 55 (0.00%)	1 / 27 (3.70%)	0 / 51 (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
Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	0 / 55 (0.00%)	0 / 27 (0.00%)	0 / 51 (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 / 55 (0.00%)	0 / 27 (0.00%)	0 / 51 (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			
Facial paralysis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 27 (0.00%)	0 / 51 (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
Hemiparesis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 27 (0.00%)	0 / 51 (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 / 55 (0.00%)	0 / 27 (0.00%)	0 / 51 (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 pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 27 (0.00%)	0 / 51 (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 / 55 (0.00%)	0 / 27 (0.00%)	0 / 51 (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			
subjects affected / exposed	1 / 55 (1.82%)	0 / 27 (0.00%)	0 / 51 (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	0 / 55 (0.00%)	0 / 27 (0.00%)	0 / 51 (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
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 27 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic congestion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 27 (0.00%)	0 / 51 (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
Uterine haemorrhage			
subjects affected / exposed	0 / 55 (0.00%)	1 / 27 (3.70%)	0 / 51 (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
Uterine polyp			
subjects affected / exposed	0 / 55 (0.00%)	0 / 27 (0.00%)	0 / 51 (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			
Asthma			

subjects affected / exposed	0 / 55 (0.00%)	0 / 27 (0.00%)	0 / 51 (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	TDF Extension From TDF + Vesatolimod 2 mg	TDF Extension from TDF + Vesatolimod 4 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 54 (9.26%)	1 / 49 (2.04%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	1 / 54 (1.85%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 54 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leiomyoma			
subjects affected / exposed	0 / 54 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	0 / 54 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 54 (1.85%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Facial paralysis			

subjects affected / exposed	1 / 54 (1.85%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 54 (1.85%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 54 (1.85%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 49 (2.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 54 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 54 (1.85%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Adenomyosis			

subjects affected / exposed	0 / 54 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic congestion			
subjects affected / exposed	1 / 54 (1.85%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine haemorrhage			
subjects affected / exposed	0 / 54 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	1 / 54 (1.85%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 54 (0.00%)	0 / 49 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	TDF + Placebo	TDF + Vesatolimod 1 mg	TDF + Vesatolimod 2 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 28 (50.00%)	25 / 53 (47.17%)	27 / 56 (48.21%)
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 28 (17.86%)	4 / 53 (7.55%)	10 / 56 (17.86%)
occurrences (all)	7	6	25
Dizziness			
subjects affected / exposed	3 / 28 (10.71%)	3 / 53 (5.66%)	1 / 56 (1.79%)
occurrences (all)	3	4	1
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	6 / 28 (21.43%)	8 / 53 (15.09%)	6 / 56 (10.71%)
occurrences (all)	7	17	6
Pyrexia			
subjects affected / exposed	1 / 28 (3.57%)	4 / 53 (7.55%)	5 / 56 (8.93%)
occurrences (all)	1	5	8
Chills			
subjects affected / exposed	1 / 28 (3.57%)	2 / 53 (3.77%)	6 / 56 (10.71%)
occurrences (all)	1	2	22
Asthenia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 53 (1.89%)	2 / 56 (3.57%)
occurrences (all)	2	1	7
Influenza like illness			
subjects affected / exposed	1 / 28 (3.57%)	1 / 53 (1.89%)	0 / 56 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 28 (10.71%)	5 / 53 (9.43%)	3 / 56 (5.36%)
occurrences (all)	5	7	4
Diarrhoea			
subjects affected / exposed	0 / 28 (0.00%)	4 / 53 (7.55%)	2 / 56 (3.57%)
occurrences (all)	0	4	3
Abdominal pain upper			
subjects affected / exposed	2 / 28 (7.14%)	3 / 53 (5.66%)	1 / 56 (1.79%)
occurrences (all)	3	3	1
Dyspepsia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 53 (1.89%)	3 / 56 (5.36%)
occurrences (all)	4	1	3
Abdominal distension			
subjects affected / exposed	2 / 28 (7.14%)	3 / 53 (5.66%)	1 / 56 (1.79%)
occurrences (all)	2	3	1
Vomiting			
subjects affected / exposed	0 / 28 (0.00%)	2 / 53 (3.77%)	0 / 56 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	3 / 53 (5.66%) 4	0 / 56 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	5 / 53 (9.43%) 7	1 / 56 (1.79%) 1
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	3 / 53 (5.66%) 3	1 / 56 (1.79%) 1
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 3	5 / 53 (9.43%) 6	4 / 56 (7.14%) 7
Arthralgia subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	3 / 53 (5.66%) 4	3 / 56 (5.36%) 3
Back pain subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	2 / 53 (3.77%) 2	4 / 56 (7.14%) 4
Pain in extremity subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	2 / 53 (3.77%) 2	3 / 56 (5.36%) 4
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 5	3 / 53 (5.66%) 3	0 / 56 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 4	2 / 53 (3.77%) 2	2 / 56 (3.57%) 2
Gingivitis subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2	0 / 53 (0.00%) 0	0 / 56 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite			

subjects affected / exposed	1 / 28 (3.57%)	1 / 53 (1.89%)	3 / 56 (5.36%)
occurrences (all)	1	1	3

Non-serious adverse events	TDF + Vesatolimod 4 mg	TDF Extension From TDF + Placebo	TDF Extension From TDF + Vesatolimod 1 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 55 (60.00%)	7 / 27 (25.93%)	14 / 51 (27.45%)
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 55 (21.82%)	0 / 27 (0.00%)	2 / 51 (3.92%)
occurrences (all)	18	0	2
Dizziness			
subjects affected / exposed	5 / 55 (9.09%)	0 / 27 (0.00%)	0 / 51 (0.00%)
occurrences (all)	6	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	14 / 55 (25.45%)	0 / 27 (0.00%)	2 / 51 (3.92%)
occurrences (all)	18	0	2
Pyrexia			
subjects affected / exposed	11 / 55 (20.00%)	0 / 27 (0.00%)	2 / 51 (3.92%)
occurrences (all)	18	0	2
Chills			
subjects affected / exposed	10 / 55 (18.18%)	0 / 27 (0.00%)	0 / 51 (0.00%)
occurrences (all)	13	0	0
Asthenia			
subjects affected / exposed	3 / 55 (5.45%)	0 / 27 (0.00%)	1 / 51 (1.96%)
occurrences (all)	12	0	1
Influenza like illness			
subjects affected / exposed	5 / 55 (9.09%)	0 / 27 (0.00%)	0 / 51 (0.00%)
occurrences (all)	13	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 55 (9.09%)	0 / 27 (0.00%)	0 / 51 (0.00%)
occurrences (all)	6	0	0
Diarrhoea			
subjects affected / exposed	5 / 55 (9.09%)	0 / 27 (0.00%)	1 / 51 (1.96%)
occurrences (all)	6	0	1

Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 27 (0.00%) 0	2 / 51 (3.92%) 2
Dyspepsia subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	1 / 27 (3.70%) 1	0 / 51 (0.00%) 0
Abdominal distension subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	0 / 27 (0.00%) 0	0 / 51 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	5 / 55 (9.09%) 5	0 / 27 (0.00%) 0	0 / 51 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 3	2 / 27 (7.41%) 2	2 / 51 (3.92%) 2
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	1 / 27 (3.70%) 1	0 / 51 (0.00%) 0
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 2	1 / 27 (3.70%) 1	0 / 51 (0.00%) 0
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	9 / 55 (16.36%) 25	0 / 27 (0.00%) 0	0 / 51 (0.00%) 0
Arthralgia subjects affected / exposed occurrences (all)	10 / 55 (18.18%) 22	0 / 27 (0.00%) 0	2 / 51 (3.92%) 2
Back pain subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 2	2 / 27 (7.41%) 2	2 / 51 (3.92%) 2
Pain in extremity subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	0 / 27 (0.00%) 0	0 / 51 (0.00%) 0

Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	4 / 55 (7.27%) 5	2 / 27 (7.41%) 3	3 / 51 (5.88%) 12
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 2	0 / 27 (0.00%) 0	5 / 51 (9.80%) 6
Gingivitis subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 27 (0.00%) 0	1 / 51 (1.96%) 1
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	0 / 27 (0.00%) 0	0 / 51 (0.00%) 0

Non-serious adverse events	TDF Extension From TDF + Vesatolimod 2 mg	TDF Extension from TDF + Vesatolimod 4 mg	
Total subjects affected by non-serious adverse events subjects affected / exposed	13 / 54 (24.07%)	12 / 49 (24.49%)	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	1 / 49 (2.04%) 1	
Dizziness subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	1 / 49 (2.04%) 1	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	1 / 54 (1.85%) 1	2 / 49 (4.08%) 2	
Pyrexia subjects affected / exposed occurrences (all)	0 / 54 (0.00%) 0	0 / 49 (0.00%) 0	
Chills subjects affected / exposed occurrences (all)	1 / 54 (1.85%) 1	0 / 49 (0.00%) 0	
Asthenia			

subjects affected / exposed	0 / 54 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Influenza like illness			
subjects affected / exposed	0 / 54 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 54 (3.70%)	0 / 49 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	1 / 54 (1.85%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Abdominal pain upper			
subjects affected / exposed	1 / 54 (1.85%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Dyspepsia			
subjects affected / exposed	1 / 54 (1.85%)	1 / 49 (2.04%)	
occurrences (all)	2	1	
Abdominal distension			
subjects affected / exposed	0 / 54 (0.00%)	2 / 49 (4.08%)	
occurrences (all)	0	2	
Vomiting			
subjects affected / exposed	0 / 54 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 54 (1.85%)	3 / 49 (6.12%)	
occurrences (all)	2	3	
Oropharyngeal pain			
subjects affected / exposed	2 / 54 (3.70%)	0 / 49 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 54 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			

Myalgia			
subjects affected / exposed	0 / 54 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Arthralgia			
subjects affected / exposed	0 / 54 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	0 / 54 (0.00%)	1 / 49 (2.04%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 54 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	4 / 54 (7.41%)	2 / 49 (4.08%)	
occurrences (all)	5	5	
Nasopharyngitis			
subjects affected / exposed	1 / 54 (1.85%)	1 / 49 (2.04%)	
occurrences (all)	1	1	
Gingivitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 49 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 54 (0.00%)	0 / 49 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 September 2015	1. References to peripheral blood mononuclear cell (PBMC) collection and associated objectives, endpoints, analysis, and storage were removed. These changes were implemented to reflect that PBMC collection would not be completed in certain countries. The original protocol (dated 21 August 2015) was applicable in countries where PBMCs were collected, and this Original 0.1 protocol was applicable in countries where PBMCs were not collected. 2. The definition of "treatment-emergent" was changed from "30 days from the last dose of study drug" to "the date of the last dose of study drug." This change was implemented to account for the treatment-free follow-up phase that began immediately after the last dose of study drug.

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/29851204>

<http://www.ncbi.nlm.nih.gov/pubmed/29505905>