



Clinical trial results:

A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Multi-center Study to Evaluate the Safety and Efficacy of GS-9620 for the Treatment of Virally-Suppressed Subjects with Chronic Hepatitis B

Summary

EudraCT number	2014-001400-22
Trial protocol	IT NL
Global end of trial date	19 October 2016

Results information

Result version number	v1
This version publication date	03 November 2017
First version publication date	03 November 2017

Trial information

Trial identification

Sponsor protocol code	GS-US-283-1059
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02166047
WHO universal trial number (UTN)	-
Other trial identifiers	ACTRN12614000628640 : ANZCTR

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Clinical Trials Mailbox , Gilead Sciences International Ltd , ClinicalTrialDisclosures@gilead.com
Scientific contact	Clinical Trials Mailbox , Gilead Sciences International Ltd , ClinicalTrialDisclosures@gilead.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 October 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	19 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the safety and tolerability of vesatolimod (GS-9620) in participants with chronic hepatitis B (CHB) infection currently being treated with oral antivirals (OAV) and to evaluate the efficacy of vesatolimod at Week 24 measured by the change from baseline in serum hepatitis B surface antigen (HBsAg) (log₁₀ IU/ml) levels.

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:

All participants continued their approved HBV oral antiviral therapy (tenofovir disoproxil fumarate (TDF), entecavir (ETV), adefovir, lamivudine, or telbivudine, either as single agents or in combination) throughout the study.

Evidence for comparator: -

Actual start date of recruitment	30 June 2014
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	Netherlands: 6
Country: Number of subjects enrolled	Italy: 28
Country: Number of subjects enrolled	United States: 43
Country: Number of subjects enrolled	Canada: 33
Country: Number of subjects enrolled	Korea, Republic of: 28
Country: Number of subjects enrolled	New Zealand: 24
Worldwide total number of subjects	162
EEA total number of subjects	34

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)	159
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States, Canada, Italy, South Korea, The Netherlands, and New Zealand. The first participant was screened on 30 June 2014. The last study visit occurred on 19 October 2016.

Pre-assignment

Screening details:

200 participants were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Vesatolimod 1 mg 4 Weeks (Cohort A)

Arm description:

Vesatolimod 1 mg tablet once a week for 4 weeks

Arm type	Experimental
Investigational medicinal product name	Vesatolimod
Investigational medicinal product code	
Other name	GS-9620
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg once a week

Arm title	Vesatolimod 2 mg 4 Weeks (Cohort A)
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Arm description:

Vesatolimod 2 mg tablet once a week for 4 weeks

Arm type	Experimental
Investigational medicinal product name	Vesatolimod
Investigational medicinal product code	
Other name	GS-9620
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2 mg once a week

Arm title	Vesatolimod 4 mg 4 Weeks (Cohort A)
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Arm description:

Vesatolimod 4 mg tablet once a week for 4 weeks

Arm type	Experimental
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Investigational medicinal product name	Vesatolimod
Investigational medicinal product code	
Other name	GS-9620
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 4 mg once a week	
Arm title	Placebo 4 Weeks (Cohort A)
Arm description: Placebo tablet once a week for 4 weeks	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Placebo once a week	
Arm title	Vesatolimod 1 mg 8 Weeks (Cohort B)
Arm description: Vesatolimod 1 mg tablet once a week for 8 weeks	
Arm type	Experimental
Investigational medicinal product name	Vesatolimod
Investigational medicinal product code	
Other name	GS-9620
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1 mg once a week	
Arm title	Vesatolimod 2 mg 8 Weeks (Cohort B)
Arm description: Vesatolimod 2 mg tablet once a week for 8 weeks	
Arm type	Experimental
Investigational medicinal product name	Vesatolimod
Investigational medicinal product code	
Other name	GS-9620
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 2 mg once a week	
Arm title	Vesatolimod 4 mg 8 Weeks (Cohort B)
Arm description: Vesatolimod 4 mg tablet once a week for 8 weeks	
Arm type	Experimental

Investigational medicinal product name	Vesatolimod
Investigational medicinal product code	
Other name	GS-9620
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 4 mg once a week	
Arm title	Placebo 8 Weeks (Cohort B)
Arm description: Placebo tablet once a week for 8 weeks	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Placebo once a week	
Arm title	Vesatolimod 1 mg 12 Weeks (Cohort C)
Arm description: Vesatolimod 1 mg tablet once a week for 12 weeks	
Arm type	Experimental
Investigational medicinal product name	Vesatolimod
Investigational medicinal product code	
Other name	GS-9620
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 1 mg once a week	
Arm title	Vesatolimod 2 mg 12 Weeks (Cohort C)
Arm description: Vesatolimod 2 mg tablet once a week for 12 weeks	
Arm type	Experimental
Investigational medicinal product name	Vesatolimod
Investigational medicinal product code	
Other name	GS-9620
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 2 mg once a week	
Arm title	Vesatolimod 4 mg 12 Weeks (Cohort C)
Arm description: Vesatolimod 4 mg tablet once a week for 12 weeks	
Arm type	Experimental

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

Dosage and administration details:

4 mg once a week

Arm title	Placebo 12 Weeks (Cohort C)
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Arm description:

Placebo tablet once a week for 12 weeks

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo once a week

Number of subjects in period 1	Vesatolimod 1 mg 4 Weeks (Cohort A)	Vesatolimod 2 mg 4 Weeks (Cohort A)	Vesatolimod 4 mg 4 Weeks (Cohort A)
Started	16	15	16
Completed	16	14	14
Not completed	0	1	2
Withdrawal By Subject	-	1	2
Adverse event, non-fatal	-	-	-

Number of subjects in period 1	Placebo 4 Weeks (Cohort A)	Vesatolimod 1 mg 8 Weeks (Cohort B)	Vesatolimod 2 mg 8 Weeks (Cohort B)
Started	5	18	17
Completed	5	17	17
Not completed	0	1	0
Withdrawal By Subject	-	-	-
Adverse event, non-fatal	-	1	-

Number of subjects in period 1	Vesatolimod 4 mg 8 Weeks (Cohort B)	Placebo 8 Weeks (Cohort B)	Vesatolimod 1 mg 12 Weeks (Cohort C)
Started	17	5	16
Completed	15	5	16
Not completed	2	0	0
Withdrawal By Subject	1	-	-
Adverse event, non-fatal	1	-	-

Number of subjects in period 1	Vesatolimod 2 mg 12 Weeks (Cohort C)	Vesatolimod 4 mg 12 Weeks (Cohort C)	Placebo 12 Weeks (Cohort C)
Started	17	14	6

Completed	17	12	6
Not completed	0	2	0
Withdrawal By Subject	-	-	-
Adverse event, non-fatal	-	2	-

Baseline characteristics

Reporting groups

Reporting group title	Vesatolimod 1 mg 4 Weeks (Cohort A)
Reporting group description: Vesatolimod 1 mg tablet once a week for 4 weeks	
Reporting group title	Vesatolimod 2 mg 4 Weeks (Cohort A)
Reporting group description: Vesatolimod 2 mg tablet once a week for 4 weeks	
Reporting group title	Vesatolimod 4 mg 4 Weeks (Cohort A)
Reporting group description: Vesatolimod 4 mg tablet once a week for 4 weeks	
Reporting group title	Placebo 4 Weeks (Cohort A)
Reporting group description: Placebo tablet once a week for 4 weeks	
Reporting group title	Vesatolimod 1 mg 8 Weeks (Cohort B)
Reporting group description: Vesatolimod 1 mg tablet once a week for 8 weeks	
Reporting group title	Vesatolimod 2 mg 8 Weeks (Cohort B)
Reporting group description: Vesatolimod 2 mg tablet once a week for 8 weeks	
Reporting group title	Vesatolimod 4 mg 8 Weeks (Cohort B)
Reporting group description: Vesatolimod 4 mg tablet once a week for 8 weeks	
Reporting group title	Placebo 8 Weeks (Cohort B)
Reporting group description: Placebo tablet once a week for 8 weeks	
Reporting group title	Vesatolimod 1 mg 12 Weeks (Cohort C)
Reporting group description: Vesatolimod 1 mg tablet once a week for 12 weeks	
Reporting group title	Vesatolimod 2 mg 12 Weeks (Cohort C)
Reporting group description: Vesatolimod 2 mg tablet once a week for 12 weeks	
Reporting group title	Vesatolimod 4 mg 12 Weeks (Cohort C)
Reporting group description: Vesatolimod 4 mg tablet once a week for 12 weeks	
Reporting group title	Placebo 12 Weeks (Cohort C)
Reporting group description: Placebo tablet once a week for 12 weeks	

Reporting group values	Vesatolimod 1 mg 4 Weeks (Cohort A)	Vesatolimod 2 mg 4 Weeks (Cohort A)	Vesatolimod 4 mg 4 Weeks (Cohort A)
Number of subjects	16	15	16
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	47 ± 7.3	50 ± 11.2	47 ± 10.0
Gender categorical Units: Subjects			
Female	1	5	4
Male	15	10	12
HBsAg Level Units: Subjects			
≤ 5000 IU/mL	13	13	13
> 5000 IU/mL	3	2	3
Hepatitis B envelope antigen (HBeAg) Status Units: Subjects			
Negative	12	11	12
Positive	4	4	4
Hepatitis B surface antigen (HBsAg) Units: log10 IU/mL arithmetic mean standard deviation	2.8 ± 0.88	3.1 ± 0.59	3.0 ± 0.70

Reporting group values	Placebo 4 Weeks (Cohort A)	Vesatolimod 1 mg 8 Weeks (Cohort B)	Vesatolimod 2 mg 8 Weeks (Cohort B)
Number of subjects	5	18	17
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	53 ± 5.3	51 ± 8.2	44 ± 9.0
Gender categorical Units: Subjects			
Female	1	9	4
Male	4	9	13
HBsAg Level Units: Subjects			
≤ 5000 IU/mL	4	15	15
> 5000 IU/mL	1	3	2
Hepatitis B envelope antigen (HBeAg) Status Units: Subjects			
Negative	4	13	14
Positive	1	5	3

Hepatitis B surface antigen (HBsAg) Units: log10 IU/mL arithmetic mean standard deviation	3.1 ± 0.69	3.1 ± 0.62	3.0 ± 0.69
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Reporting group values	Vesatolimod 4 mg 8 Weeks (Cohort B)	Placebo 8 Weeks (Cohort B)	Vesatolimod 1 mg 12 Weeks (Cohort C)
Number of subjects	17	5	16
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	44 ± 11.1	53 ± 5.4	48 ± 9.8
Gender categorical Units: Subjects			
Female	4	1	5
Male	13	4	11
HBsAg Level Units: Subjects			
≤ 5000 IU/mL	14	5	14
> 5000 IU/mL	3	0	2
Hepatitis B envelope antigen (HBeAg) Status Units: Subjects			
Negative	14	5	13
Positive	3	0	3
Hepatitis B surface antigen (HBsAg) Units: log10 IU/mL arithmetic mean standard deviation	3.1 ± 0.90	2.7 ± 0.73	3.3 ± 0.45

Reporting group values	Vesatolimod 2 mg 12 Weeks (Cohort C)	Vesatolimod 4 mg 12 Weeks (Cohort C)	Placebo 12 Weeks (Cohort C)
Number of subjects	17	14	6
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	48 ± 9.7	50 ± 11.6	46 ± 10.9
Gender categorical Units: Subjects			
Female	2	3	0
Male	15	11	6
HBsAg Level Units: Subjects			
≤ 5000 IU/mL	15	13	5
> 5000 IU/mL	2	1	1

Hepatitis B envelope antigen (HBeAg) Status Units: Subjects			
Negative	14	12	4
Positive	3	2	2
Hepatitis B surface antigen (HBsAg) Units: log10 IU/mL arithmetic mean standard deviation	3.0 ± 0.54	3.0 ± 0.69	2.4 ± 1.01

Reporting group values	Total		
Number of subjects	162		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	39		
Male	123		
HBsAg Level Units: Subjects			
≤ 5000 IU/mL	139		
> 5000 IU/mL	23		
Hepatitis B envelope antigen (HBeAg) Status Units: Subjects			
Negative	128		
Positive	34		
Hepatitis B surface antigen (HBsAg) Units: log10 IU/mL arithmetic mean standard deviation	-		

End points

End points reporting groups

Reporting group title	Vesatolimod 1 mg 4 Weeks (Cohort A)
Reporting group description: Vesatolimod 1 mg tablet once a week for 4 weeks	
Reporting group title	Vesatolimod 2 mg 4 Weeks (Cohort A)
Reporting group description: Vesatolimod 2 mg tablet once a week for 4 weeks	
Reporting group title	Vesatolimod 4 mg 4 Weeks (Cohort A)
Reporting group description: Vesatolimod 4 mg tablet once a week for 4 weeks	
Reporting group title	Placebo 4 Weeks (Cohort A)
Reporting group description: Placebo tablet once a week for 4 weeks	
Reporting group title	Vesatolimod 1 mg 8 Weeks (Cohort B)
Reporting group description: Vesatolimod 1 mg tablet once a week for 8 weeks	
Reporting group title	Vesatolimod 2 mg 8 Weeks (Cohort B)
Reporting group description: Vesatolimod 2 mg tablet once a week for 8 weeks	
Reporting group title	Vesatolimod 4 mg 8 Weeks (Cohort B)
Reporting group description: Vesatolimod 4 mg tablet once a week for 8 weeks	
Reporting group title	Placebo 8 Weeks (Cohort B)
Reporting group description: Placebo tablet once a week for 8 weeks	
Reporting group title	Vesatolimod 1 mg 12 Weeks (Cohort C)
Reporting group description: Vesatolimod 1 mg tablet once a week for 12 weeks	
Reporting group title	Vesatolimod 2 mg 12 Weeks (Cohort C)
Reporting group description: Vesatolimod 2 mg tablet once a week for 12 weeks	
Reporting group title	Vesatolimod 4 mg 12 Weeks (Cohort C)
Reporting group description: Vesatolimod 4 mg tablet once a week for 12 weeks	
Reporting group title	Placebo 12 Weeks (Cohort C)
Reporting group description: Placebo tablet once a week for 12 weeks	

Primary: Mean Change in Serum Hepatitis B Surface Antigen (HBsAg) (log10 IU/ml) at Week 24

End point title	Mean Change in Serum Hepatitis B Surface Antigen (HBsAg) (log10 IU/ml) at Week 24
End point description: Participants in the Full Analysis Set (participants who were randomized and received at least 1 dose of study drug) with available data were analyzed.	
End point type	Primary
End point timeframe: Baseline; Week 24	

End point values	Vesatolimod 1 mg 4 Weeks (Cohort A)	Vesatolimod 2 mg 4 Weeks (Cohort A)	Vesatolimod 4 mg 4 Weeks (Cohort A)	Placebo 4 Weeks (Cohort A)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	14	15	5
Units: log10 IU/mL				
least squares mean (confidence interval 95%)	-0.011 (-0.054 to 0.031)	0.033 (-0.012 to 0.079)	-0.018 (-0.062 to 0.026)	-0.035 (-0.109 to 0.040)

End point values	Vesatolimod 1 mg 8 Weeks (Cohort B)	Vesatolimod 2 mg 8 Weeks (Cohort B)	Vesatolimod 4 mg 8 Weeks (Cohort B)	Placebo 8 Weeks (Cohort B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	17	16	5
Units: log10 IU/mL				
least squares mean (confidence interval 95%)	-0.081 (-0.145 to -0.016)	-0.081 (-0.147 to -0.014)	-0.082 (-0.148 to -0.015)	-0.163 (-0.281 to -0.045)

End point values	Vesatolimod 1 mg 12 Weeks (Cohort C)	Vesatolimod 2 mg 12 Weeks (Cohort C)	Vesatolimod 4 mg 12 Weeks (Cohort C)	Placebo 12 Weeks (Cohort C)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	17	12	6
Units: log10 IU/mL				
least squares mean (confidence interval 95%)	-0.015 (-0.057 to 0.027)	0.000 (-0.041 to 0.042)	0.000 (-0.046 to 0.047)	0.001 (-0.057 to 0.058)

Statistical analyses

Statistical analysis title	Treatment Diff (vesatolimod 1 mg 4 wk vs placebo)
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Statistical analysis description:

A mixed effect model for repeated measures (MMRM) was used to analyze HBsAg change from baseline, which included treatment, baseline HBsAg level (> 5000 IU/mL or ≤ 5000 IU/mL), HBeAg baseline status (positive or negative), visit and treatment-by-visit interaction as fixed effect and visit as repeated

measurement.

Comparison groups	Vesatolimod 1 mg 4 Weeks (Cohort A) v Placebo 4 Weeks (Cohort A)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	= 0.59 ^[2]
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Mean
Point estimate	0.023
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.061
upper limit	0.108

Notes:

[1] - Statistical comparison

[2] - P-values between treatment groups with placebo were not adjusted for multiplicity due to exploratory nature of the study.

Statistical analysis title	Treatment Diff (vesatolimod 2 mg 4 wk vs placebo)
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Statistical analysis description:

A MMRM was used to analyze HBsAg change from baseline, which included treatment, baseline HBsAg level (> 5000 IU/mL or ≤ 5000 IU/mL), HBeAg baseline status (positive or negative), visit and treatment-by-visit interaction as fixed effect and visit as repeated measurement.

Comparison groups	Vesatolimod 2 mg 4 Weeks (Cohort A) v Placebo 4 Weeks (Cohort A)
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	other ^[3]
P-value	= 0.12 ^[4]
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Mean
Point estimate	0.068
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.018
upper limit	0.154

Notes:

[3] - Statistical comparison

[4] - P-values between treatment groups with placebo were not adjusted for multiplicity due to exploratory nature of the study.

Statistical analysis title	Treatment Diff (vesatolimod 4 mg 4 wk vs placebo)
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Statistical analysis description:

A MMRM was used to analyze HBsAg change from baseline, which included treatment, baseline HBsAg level (> 5000 IU/mL or ≤ 5000 IU/mL), HBeAg baseline status (positive or negative), visit and treatment-by-visit interaction as fixed effect and visit as repeated measurement.

Comparison groups	Vesatolimod 4 mg 4 Weeks (Cohort A) v Placebo 4 Weeks (Cohort A)
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Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other ^[5]
P-value	= 0.701 ^[6]
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Mean
Point estimate	0.017
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.069
upper limit	0.102

Notes:

[5] - Statistical comparison

[6] - P-values between treatment groups with placebo were not adjusted for multiplicity due to exploratory nature of the study.

Statistical analysis title	Treatment Diff (vesatolimod 1 mg 8 wk vs placebo)
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Statistical analysis description:

A MMRM was used to analyze HBsAg change from baseline, which included treatment, baseline HBsAg level (> 5000 IU/mL or ≤ 5000 IU/mL), HBeAg baseline status (positive or negative), visit and treatment-by-visit interaction as fixed effect and visit as repeated measurement.

Comparison groups	Vesatolimod 1 mg 8 Weeks (Cohort B) v Placebo 8 Weeks (Cohort B)
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other ^[7]
P-value	= 0.21 ^[8]
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Mean
Point estimate	0.082
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.046
upper limit	0.21

Notes:

[7] - Statistical comparison

[8] - P-values between treatment groups with placebo were not adjusted for multiplicity due to exploratory nature of the study.

Statistical analysis title	Treatment Diff (vesatolimod 2 mg 8 wk vs placebo)
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Statistical analysis description:

A MMRM was used to analyze HBsAg change from baseline, which included treatment, baseline HBsAg level (> 5000 IU/mL or ≤ 5000 IU/mL), HBeAg baseline status (positive or negative), visit and treatment-by-visit interaction as fixed effect and visit as repeated measurement.

Comparison groups	Vesatolimod 2 mg 8 Weeks (Cohort B) v Placebo 8 Weeks (Cohort B)
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Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other ^[9]
P-value	= 0.207 ^[10]
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Mean
Point estimate	0.082
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.046
upper limit	0.21

Notes:

[9] - Statistical comparison

[10] - P-values between treatment groups with placebo were not adjusted for multiplicity due to exploratory nature of the study.

Statistical analysis title	Treatment Diff (vesatolimod 4 mg 8 wk vs placebo)
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Statistical analysis description:

A MMRM was used to analyze HBsAg change from baseline, which included treatment, baseline HBsAg level (> 5000 IU/mL or ≤ 5000 IU/mL), HBeAg baseline status (positive or negative), visit and treatment-by-visit interaction as fixed effect and visit as repeated measurement.

Comparison groups	Vesatolimod 4 mg 8 Weeks (Cohort B) v Placebo 8 Weeks (Cohort B)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other ^[11]
P-value	= 0.216 ^[12]
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Mean
Point estimate	0.081
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.048
upper limit	0.21

Notes:

[11] - Statistical comparison

[12] - P-values between treatment groups with placebo were not adjusted for multiplicity due to exploratory nature of the study.

Statistical analysis title	Treatment Diff (vesatolimod 1 mg 12 wk vs placebo)
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Statistical analysis description:

A MMRM was used to analyze HBsAg change from baseline, which included treatment, baseline HBsAg level (> 5000 IU/mL or ≤ 5000 IU/mL), HBeAg baseline status (positive or negative), visit and treatment-by-visit interaction as fixed effect and visit as repeated measurement.

Comparison groups	Vesatolimod 1 mg 12 Weeks (Cohort C) v Placebo 12 Weeks (Cohort C)
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Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	other ^[13]
P-value	= 0.652 ^[14]
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Mean
Point estimate	-0.015
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.081
upper limit	0.051

Notes:

[13] - Statistical comparison

[14] - P-values between treatment groups with placebo were not adjusted for multiplicity due to exploratory nature of the study.

Statistical analysis title	Treatment Diff (vesatolimod 2 mg 12 wk vs placebo)
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Statistical analysis description:

A MMRM was used to analyze HBsAg change from baseline, which included treatment, baseline HBsAg level (> 5000 IU/mL or ≤ 5000 IU/mL), HBeAg baseline status (positive or negative), visit and treatment-by-visit interaction as fixed effect and visit as repeated measurement.

Comparison groups	Vesatolimod 2 mg 12 Weeks (Cohort C) v Placebo 12 Weeks (Cohort C)
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other ^[15]
P-value	= 0.994 ^[16]
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Mean
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.066
upper limit	0.065

Notes:

[15] - Statistical comparison

[16] - P-values between treatment groups with placebo were not adjusted for multiplicity due to exploratory nature of the study.

Statistical analysis title	Treatment Diff (vesatolimod 4 mg 12 wk vs placebo)
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Statistical analysis description:

A MMRM was used to analyze HBsAg change from baseline, which included treatment, baseline HBsAg level (> 5000 IU/mL or ≤ 5000 IU/mL), HBeAg baseline status (positive or negative), visit and treatment-by-visit interaction as fixed effect and visit as repeated measurement.

Comparison groups	Vesatolimod 4 mg 12 Weeks (Cohort C) v Placebo 12 Weeks (Cohort C)
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Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	other ^[17]
P-value	= 0.996 ^[18]
Method	Mixed models analysis
Parameter estimate	Difference in Least Square Mean
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.069
upper limit	0.069

Notes:

[17] - Statistical comparison

[18] - P-values between treatment groups with placebo were not adjusted for multiplicity due to exploratory nature of the study.

Secondary: Proportion of Participants With HBeAg Loss and Seroconversion

End point title	Proportion of Participants With HBeAg Loss and Seroconversion
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End point description:

HBeAg loss is defined as qualitative HBeAg result changing from positive at baseline to negative at any postbaseline visit within the targeted time window.

HBeAg seroconversion is defined as qualitative HBeAb result changing from negative at baseline to positive at any postbaseline visit within the targeted time window.

Participants who have missing information were assumed to have no HBeAg loss and no HBeAg seroconversion.

Only participants who were HBeAg+ at baseline were included.

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

End point type	Secondary
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End point timeframe:

Weeks 24 and 48

End point values	Vesatolimod 1 mg 4 Weeks (Cohort A)	Vesatolimod 2 mg 4 Weeks (Cohort A)	Vesatolimod 4 mg 4 Weeks (Cohort A)	Placebo 4 Weeks (Cohort A)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	4	1
Units: percentage of participants				
number (not applicable)				
Week 24	0	0	0	0
Week 48	0	0	0	0

End point values	Vesatolimod 1 mg 8 Weeks (Cohort B)	Vesatolimod 2 mg 8 Weeks (Cohort B)	Vesatolimod 4 mg 8 Weeks (Cohort B)	Placebo 8 Weeks (Cohort B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	0 ^[19]
Units: percentage of participants				
number (not applicable)				

Week 24	20.0	0	0	
Week 48	20.0	0	0	

Notes:

[19] - No participants in this group had HBeAg+ at baseline.

End point values	Vesatolimod 1 mg 12 Weeks (Cohort C)	Vesatolimod 2 mg 12 Weeks (Cohort C)	Vesatolimod 4 mg 12 Weeks (Cohort C)	Placebo 12 Weeks (Cohort C)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	2	2
Units: percentage of participants				
number (not applicable)				
Week 24	0	0	0	0
Week 48	33.3	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants With HBsAg Loss and Seroconversion

End point title	Proportion of Participants With HBsAg Loss and Seroconversion
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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 within the targeted time window.

HBsAg seroconversion was defined as qualitative HBsAb result changing from negative at baseline to positive at any postbaseline visit within the targeted time window.

Participants who have missing information were assumed to have no HBsAg loss and no HBsAg seroconversion.

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

End point type	Secondary
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End point timeframe:

Weeks 24 and 48

End point values	Vesatolimod 1 mg 4 Weeks (Cohort A)	Vesatolimod 2 mg 4 Weeks (Cohort A)	Vesatolimod 4 mg 4 Weeks (Cohort A)	Placebo 4 Weeks (Cohort A)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	16	5
Units: percentage of participants				
number (not applicable)				
Week 24	0	0	0	0
Week 48	0	0	0	0

End point values	Vesatolimod 1 mg 8 Weeks	Vesatolimod 2 mg 8 Weeks	Vesatolimod 4 mg 8 Weeks	Placebo 8 Weeks (Cohort A)
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	(Cohort B)	(Cohort B)	(Cohort B)	B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	17	17	5
Units: percentage of participants				
number (not applicable)				
Week 24	0	0	0	0
Week 48	0	0	0	0

End point values	Vesatolimod 1 mg 12 Weeks (Cohort C)	Vesatolimod 2 mg 12 Weeks (Cohort C)	Vesatolimod 4 mg 12 Weeks (Cohort C)	Placebo 12 Weeks (Cohort C)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	17	14	6
Units: percentage of participants				
number (not applicable)				
Week 24	0	0	0	0
Week 48	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in log10 IU/ml Serum HBsAg at Week 4

End point title	Mean Change in log10 IU/ml Serum HBsAg at Week 4
End point description:	Participants in the Full Analysis Set with available data were analyzed.
End point type	Secondary
End point timeframe:	
Baseline; Week 4	

End point values	Vesatolimod 1 mg 4 Weeks (Cohort A)	Vesatolimod 2 mg 4 Weeks (Cohort A)	Vesatolimod 4 mg 4 Weeks (Cohort A)	Placebo 4 Weeks (Cohort A)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	14	14	5
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-0.009 (± 0.0505)	0.025 (± 0.0514)	-0.008 (± 0.0516)	-0.017 (± 0.0600)

End point values	Vesatolimod 1 mg 8 Weeks (Cohort B)	Vesatolimod 2 mg 8 Weeks (Cohort B)	Vesatolimod 4 mg 8 Weeks (Cohort B)	Placebo 8 Weeks (Cohort B)
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Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	17	17	5
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-0.003 (\pm 0.0574)	0.014 (\pm 0.0794)	-0.001 (\pm 0.0436)	0.046 (\pm 0.0648)

End point values	Vesatolimod 1 mg 12 Weeks (Cohort C)	Vesatolimod 2 mg 12 Weeks (Cohort C)	Vesatolimod 4 mg 12 Weeks (Cohort C)	Placebo 12 Weeks (Cohort C)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	17	13	6
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-0.034 (\pm 0.0375)	-0.023 (\pm 0.0529)	-0.001 (\pm 0.0627)	-0.041 (\pm 0.0955)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in log10 IU/ml Serum HBsAg at Week 8

End point title	Mean Change in log10 IU/ml Serum HBsAg at Week 8
End point description:	Participants in the Full Analysis Set with available data were analyzed.
End point type	Secondary
End point timeframe:	
Baseline; Week 8	

End point values	Vesatolimod 1 mg 4 Weeks (Cohort A)	Vesatolimod 2 mg 4 Weeks (Cohort A)	Vesatolimod 4 mg 4 Weeks (Cohort A)	Placebo 4 Weeks (Cohort A)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	13	15	4
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-0.029 (\pm 0.0666)	0.002 (\pm 0.0544)	-0.035 (\pm 0.0649)	-0.013 (\pm 0.0440)

End point values	Vesatolimod 1 mg 8 Weeks (Cohort B)	Vesatolimod 2 mg 8 Weeks (Cohort B)	Vesatolimod 4 mg 8 Weeks (Cohort B)	Placebo 8 Weeks (Cohort B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	17	17	4
Units: log10 IU/mL				
arithmetic mean (standard deviation)	0.000 (\pm 0.0442)	0.006 (\pm 0.0772)	0.020 (\pm 0.0596)	0.006 (\pm 0.0600)

End point values	Vesatolimod 1 mg 12 Weeks (Cohort C)	Vesatolimod 2 mg 12 Weeks (Cohort C)	Vesatolimod 4 mg 12 Weeks (Cohort C)	Placebo 12 Weeks (Cohort C)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	17	12	6
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-0.021 (\pm 0.0376)	-0.033 (\pm 0.0487)	-0.013 (\pm 0.0426)	-0.019 (\pm 0.0483)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in log10 IU/ml Serum HBsAg at Week 12

End point title	Mean Change in log10 IU/ml Serum HBsAg at Week 12
End point description:	Participants in the Full Analysis Set with available data were analyzed.
End point type	Secondary
End point timeframe:	Baseline; Week 12

End point values	Vesatolimod 1 mg 4 Weeks (Cohort A)	Vesatolimod 2 mg 4 Weeks (Cohort A)	Vesatolimod 4 mg 4 Weeks (Cohort A)	Placebo 4 Weeks (Cohort A)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	14	15	5
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-0.050 (\pm 0.0755)	0.017 (\pm 0.0646)	-0.004 (\pm 0.0546)	-0.023 (\pm 0.0623)

End point values	Vesatolimod 1 mg 8 Weeks (Cohort B)	Vesatolimod 2 mg 8 Weeks (Cohort B)	Vesatolimod 4 mg 8 Weeks (Cohort B)	Placebo 8 Weeks (Cohort B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	17	16	5
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-0.031 (\pm 0.0817)	-0.005 (\pm 0.0843)	-0.021 (\pm 0.0716)	-0.020 (\pm 0.0666)

End point values	Vesatolimod 1 mg 12 Weeks	Vesatolimod 2 mg 12 Weeks	Vesatolimod 4 mg 12 Weeks	Placebo 12 Weeks (Cohort C)
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	(Cohort C)	(Cohort C)	(Cohort C)	C)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	16	12	6
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-0.023 (\pm 0.0545)	-0.034 (\pm 0.0549)	-0.010 (\pm 0.0621)	-0.024 (\pm 0.0661)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in log10 IU/ml Serum HBsAg at Week 48

End point title	Mean Change in log10 IU/ml Serum HBsAg at Week 48
End point description:	Participants in the Full Analysis Set with available data were analyzed.
End point type	Secondary
End point timeframe:	
Baseline; Week 48	

End point values	Vesatolimod 1 mg 4 Weeks (Cohort A)	Vesatolimod 2 mg 4 Weeks (Cohort A)	Vesatolimod 4 mg 4 Weeks (Cohort A)	Placebo 4 Weeks (Cohort A)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	13	14	4
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-0.048 (\pm 0.1054)	-0.055 (\pm 0.1400)	-0.071 (\pm 0.0857)	-0.067 (\pm 0.0831)

End point values	Vesatolimod 1 mg 8 Weeks (Cohort B)	Vesatolimod 2 mg 8 Weeks (Cohort B)	Vesatolimod 4 mg 8 Weeks (Cohort B)	Placebo 8 Weeks (Cohort B)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	16	15	5
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-0.035 (\pm 0.0923)	-0.024 (\pm 0.0679)	-0.114 (\pm 0.2169)	-0.324 (\pm 0.6811)

End point values	Vesatolimod 1 mg 12 Weeks (Cohort C)	Vesatolimod 2 mg 12 Weeks (Cohort C)	Vesatolimod 4 mg 12 Weeks (Cohort C)	Placebo 12 Weeks (Cohort C)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	17	12	6
Units: log10 IU/mL				
arithmetic mean (standard deviation)	-0.083 (\pm)	-0.071 (\pm)	-0.054 (\pm)	-0.063 (\pm)

0.0858)	0.1076)	0.0715)	0.1011)
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 12 weeks plus 30 days

Adverse event reporting additional description:

Safety Analysis Set: participants who received at least 1 dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	Vesatolimod 1 mg 4 Weeks (Cohort A)
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Reporting group description:

Vesatolimod 1 mg tablet once a week for 4 weeks

Reporting group title	Vesatolimod 2 mg 4 Weeks (Cohort A)
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Reporting group description:

Vesatolimod 2 mg tablet once a week for 4 weeks

Reporting group title	Vesatolimod 4 mg 4 Weeks (Cohort A)
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Reporting group description:

Vesatolimod 4 mg tablet once a week for 4 weeks

Reporting group title	Placebo 4 Weeks (Cohort A)
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Reporting group description:

Placebo tablet once a week for 4 weeks

Reporting group title	Vesatolimod 1 mg 8 Weeks (Cohort B)
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Reporting group description:

Vesatolimod 1 mg tablet once a week for 8 weeks

Reporting group title	Vesatolimod 2 mg 8 Weeks (Cohort B)
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Reporting group description:

Vesatolimod 2 mg tablet once a week for 8 weeks

Reporting group title	Vesatolimod 4 mg 8 Weeks (Cohort B)
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Reporting group description:

Vesatolimod 4 mg tablet once a week for 8 weeks

Reporting group title	Placebo 8 Weeks (Cohort B)
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Reporting group description:

Placebo tablet once a week for 8 weeks

Reporting group title	Vesatolimod 1 mg 12 Weeks (Cohort C)
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Reporting group description:

Vesatolimod 1 mg tablet once a week for 12 weeks

Reporting group title	Vesatolimod 2 mg 12 Weeks (Cohort C)
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Reporting group description:

Vesatolimod 2 mg tablet once a week for 12 weeks

Reporting group title	Vesatolimod 4 mg 12 Weeks (Cohort C)
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Reporting group description:

Vesatolimod 4 mg tablet once a week for 12 weeks

Reporting group title	Placebo 12 Weeks (Cohort C)
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Reporting group description:

Placebo tablet once a week for 12 weeks

Serious adverse events	Vesatolimod 1 mg 4 Weeks (Cohort A)	Vesatolimod 2 mg 4 Weeks (Cohort A)	Vesatolimod 4 mg 4 Weeks (Cohort A)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	1 / 16 (6.25%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Eye disorders			
Cataract			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (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			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (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	Placebo 4 Weeks (Cohort A)	Vesatolimod 1 mg 8 Weeks (Cohort B)	Vesatolimod 2 mg 8 Weeks (Cohort B)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (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
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (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			
Headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (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
Tremor			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (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			

Chills			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (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 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (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			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (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	Vesatolimod 4 mg 8 Weeks (Cohort B)	Placebo 8 Weeks (Cohort B)	Vesatolimod 1 mg 12 Weeks (Cohort C)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (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
Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (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			
Headache			

subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (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
Tremor			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (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			
Chills			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (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 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (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			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (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	Vesatolimod 2 mg 12 Weeks (Cohort C)	Vesatolimod 4 mg 12 Weeks (Cohort C)	Placebo 12 Weeks (Cohort C)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 17 (5.88%)	1 / 14 (7.14%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hot flush			

subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (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
Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (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			
Headache			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (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
Tremor			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (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			
Chills			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (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 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (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
Eye disorders			
Cataract			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	0 / 6 (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			

subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Vesatolimod 1 mg 4 Weeks (Cohort A)	Vesatolimod 2 mg 4 Weeks (Cohort A)	Vesatolimod 4 mg 4 Weeks (Cohort A)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 16 (62.50%)	12 / 15 (80.00%)	13 / 16 (81.25%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of liver			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	4 / 16 (25.00%)	3 / 15 (20.00%)	3 / 16 (18.75%)
occurrences (all)	4	3	3
Feeling cold			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Feeling hot			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Mucosal dryness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	3 / 16 (18.75%)
occurrences (all)	3	0	4
Thirst			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Pollakiuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Erectile dysfunction			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nasal obstruction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Pharyngeal oedema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Sneezing			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Initial insomnia			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Insomnia			
subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Irritability			
subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Middle insomnia			
subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Panic attack			
subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Investigations			
Amylase increased			
subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Blood pressure abnormal			
subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Lipase increased			
subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Weight decreased			
subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	1 / 16 (6.25%) 1
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Fall			
subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Nervous system disorders			

Disturbance in attention subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	1 / 16 (6.25%) 1
Dizziness subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 2	1 / 15 (6.67%) 1	0 / 16 (0.00%) 0
Dizziness postural subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Dysgeusia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	0 / 16 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 3	3 / 15 (20.00%) 4	2 / 16 (12.50%) 2
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Mental impairment subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Parosmia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Somnolence subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Ear and labyrinth disorders			
Ear swelling subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Vertigo positional subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	0 / 16 (0.00%) 0
Eye disorders			

Asthenopia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Glaucoma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dental caries			

subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	1 / 16 (6.25%)
occurrences (all)	2	1	1
Epigastric discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Mouth cyst			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Paraesthesia oral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Abdominal pain lower			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nail growth abnormal			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Pruritus generalised			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rash papular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chromaturia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Micturition frequency decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Muscle fatigue			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Neck pain			

subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Diverticulitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Oral pustule			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Root canal infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Iron deficiency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	2
Bone pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Bursitis			

subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo 4 Weeks (Cohort A)	Vesatolimod 1 mg 8 Weeks (Cohort B)	Vesatolimod 2 mg 8 Weeks (Cohort B)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)	12 / 18 (66.67%)	7 / 17 (41.18%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of liver			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	1 / 17 (5.88%)
occurrences (all)	0	1	3
Fatigue			
subjects affected / exposed	1 / 5 (20.00%)	2 / 18 (11.11%)	0 / 17 (0.00%)
occurrences (all)	1	2	0
Feeling cold			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0

Malaise			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Mucosal dryness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Thirst			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Pollakiuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Erectile dysfunction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Nasal obstruction			

subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	2 / 18 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	3	0
Pharyngeal oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Sneezing			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	1 / 5 (20.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Initial insomnia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 5 (20.00%)	2 / 18 (11.11%)	0 / 17 (0.00%)
occurrences (all)	1	2	0
Irritability			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0

Middle insomnia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0
Panic attack subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Investigations			
Amylase increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Blood pressure abnormal subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Lipase increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Injury, poisoning and procedural complications			
Arthropod bite subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Nervous system disorders			
Disturbance in attention subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	2 / 18 (11.11%) 2	2 / 17 (11.76%) 2
Dizziness postural subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0

Dysgeusia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	2 / 5 (40.00%)	6 / 18 (33.33%)	2 / 17 (11.76%)
occurrences (all)	2	7	3
Hypoaesthesia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Mental impairment			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Parosmia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vertigo positional			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Asthenopia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Glaucoma			

subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Epigastric discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Mouth cyst			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	3 / 18 (16.67%)	0 / 17 (0.00%)
occurrences (all)	0	4	0
Paraesthesia oral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 5 (0.00%)	2 / 18 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Alopecia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Dermatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Nail growth abnormal			

subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Micturition frequency decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Muscle fatigue			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Neck pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Osteoarthritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Temporomandibular joint syndrome subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Diverticulitis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Gastroenteritis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1
Gingivitis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Influenza subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0
Oral herpes subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Oral pustule subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Pharyngitis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Respiratory tract infection viral subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Rhinitis			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Root canal infection subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 18 (5.56%) 1	1 / 17 (5.88%) 1
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0
Iron deficiency subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Bone pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1
Bursitis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0

Non-serious adverse events	Vesatolimod 4 mg 8 Weeks (Cohort B)	Placebo 8 Weeks (Cohort B)	Vesatolimod 1 mg 12 Weeks (Cohort C)
Total subjects affected by non-serious adverse events subjects affected / exposed	10 / 17 (58.82%)	4 / 5 (80.00%)	12 / 16 (75.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Haemangioma of liver subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 5 (20.00%) 1	0 / 16 (0.00%) 0
Vascular disorders			

Haematoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 5 (20.00%)	2 / 16 (12.50%)
occurrences (all)	1	1	2
Chills			
subjects affected / exposed	1 / 17 (5.88%)	1 / 5 (20.00%)	0 / 16 (0.00%)
occurrences (all)	2	1	0
Fatigue			
subjects affected / exposed	2 / 17 (11.76%)	1 / 5 (20.00%)	4 / 16 (25.00%)
occurrences (all)	2	1	4
Feeling cold			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	2 / 17 (11.76%)	0 / 5 (0.00%)	4 / 16 (25.00%)
occurrences (all)	3	0	4
Malaise			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Mucosal dryness			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pain			

subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 5 (20.00%)	2 / 16 (12.50%)
occurrences (all)	2	1	4
Thirst			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Pollakiuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Erectile dysfunction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Nasal congestion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nasal obstruction			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Pharyngeal oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rhinitis allergic			

subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Rhinorrhoea			
subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Sneezing			
subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Throat irritation			
subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Psychiatric disorders			
Agitation			
subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Anxiety			
subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 2	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Initial insomnia			
subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Insomnia			
subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Irritability			
subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Middle insomnia			
subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Panic attack			
subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Investigations			
Amylase increased			

subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Blood pressure abnormal subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	1 / 16 (6.25%) 1
Lipase increased subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Injury, poisoning and procedural complications			
Arthropod bite subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Nervous system disorders			
Disturbance in attention subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Dizziness postural subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	1 / 16 (6.25%) 1
Dysgeusia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	4 / 17 (23.53%) 4	2 / 5 (40.00%) 2	4 / 16 (25.00%) 5
Hypoaesthesia			

subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Mental impairment subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Parosmia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Somnolence subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	2 / 16 (12.50%) 2
Ear and labyrinth disorders Ear swelling subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Vertigo positional subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Eye disorders Asthenopia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Diplopia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Dry eye subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Glaucoma subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Photophobia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 5 (20.00%) 1	0 / 16 (0.00%) 0
Photopsia			

subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Vitreous floaters subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Visual acuity reduced subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Gastrointestinal disorders			
Abdominal distension subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Dental caries subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Epigastric discomfort subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Haemorrhoids subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Mouth cyst subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	1 / 16 (6.25%) 1
Mouth ulceration subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0

Nausea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Paraesthesia oral			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nail growth abnormal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			

subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Psoriasis			
subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Rash erythematous			
subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Rash maculo-papular			
subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Rash papular			
subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Urticaria			
subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 5 (20.00%) 1	0 / 16 (0.00%) 0
Micturition frequency decreased			
subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 5 (20.00%) 1	0 / 16 (0.00%) 0
Nocturia			
subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	1 / 5 (20.00%) 1	0 / 16 (0.00%) 0
Flank pain			
subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Muscle fatigue			

subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	4	0	3
Neck pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Diverticulitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 17 (5.88%)	1 / 5 (20.00%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Oral herpes			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Oral pustule			
subjects affected / exposed	0 / 17 (0.00%)	1 / 5 (20.00%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Root canal infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 5 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Iron deficiency subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 5 (20.00%) 1	0 / 16 (0.00%) 0
Bone pain subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	0 / 16 (0.00%) 0
Bursitis subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 5 (0.00%) 0	1 / 16 (6.25%) 1

Non-serious adverse events	Vesatolimod 2 mg 12 Weeks (Cohort C)	Vesatolimod 4 mg 12 Weeks (Cohort C)	Placebo 12 Weeks (Cohort C)
Total subjects affected by non-serious adverse events subjects affected / exposed	12 / 17 (70.59%)	9 / 14 (64.29%)	3 / 6 (50.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Haemangioma of liver subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Vascular disorders			
Haematoma subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 14 (7.14%) 1	0 / 6 (0.00%) 0
Hypertension subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	1 / 17 (5.88%)	5 / 14 (35.71%)	0 / 6 (0.00%)
occurrences (all)	3	17	0
Chills			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 17 (11.76%)	1 / 14 (7.14%)	1 / 6 (16.67%)
occurrences (all)	2	1	1
Feeling cold			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Feeling hot			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 17 (0.00%)	3 / 14 (21.43%)	0 / 6 (0.00%)
occurrences (all)	0	8	0
Malaise			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Mucosal dryness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	1 / 17 (5.88%)	3 / 14 (21.43%)	1 / 6 (16.67%)
occurrences (all)	1	6	1
Thirst			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Vessel puncture site bruise subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Reproductive system and breast disorders			
Pollakiuria subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Erectile dysfunction subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Nasal congestion subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Nasal obstruction subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Pharyngeal oedema subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Sneezing subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Throat irritation			

subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Initial insomnia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Irritability			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Middle insomnia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Panic attack			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Investigations			
Amylase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Blood pressure abnormal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	2
Weight decreased			

subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dizziness postural			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	3 / 17 (17.65%)	3 / 14 (21.43%)	3 / 6 (50.00%)
occurrences (all)	3	8	4
Hypoaesthesia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Mental impairment			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Somnolence			

subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 14 (0.00%) 0	0 / 6 (0.00%) 0
Ear and labyrinth disorders			
Ear swelling			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vertigo positional			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Asthenopia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Diplopia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Glaucoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vitreous floaters			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Visual acuity reduced			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			

Abdominal distension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	3 / 17 (17.65%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	3	1	0
Dental caries			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Epigastric discomfort			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Mouth cyst			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Paraesthesia oral			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Toothache			
subjects affected / exposed	1 / 17 (5.88%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nail growth abnormal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psoriasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			

subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Micturition frequency decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle fatigue			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			

subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 17 (0.00%)	2 / 14 (14.29%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Neck pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Spinal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Diverticulitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Influenza			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oral pustule			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Root canal infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 17 (0.00%)	1 / 14 (7.14%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Iron deficiency			

subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Bone pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 14 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 April 2014	<ul style="list-style-type: none">• Subject visits were restructured to align with data analysis objectives.• The background section was updated.• The exploratory objectives were clarified.• Expectations for pharmacogenomics and pharmacokinetic substudies were clarified.• The screening window was increased from 28 days to 45 days and rescreening requirements were clarified.• One inclusion criterion was updated based upon new laboratory standards.• One exclusion criterion was updated based upon Food and Drug Administration (FDA) feedback regarding liver cirrhosis and bridging fibrosis.• The study drug description, handling, dosage, and administration sections were clarified due to multiple supplies of study drug.• The description of dose-limiting toxicities and discontinuation events were revised.
19 February 2015	<ul style="list-style-type: none">• Addition of quality of life (QOL) surveys (Short Form 36 [SF-36], Chronic Liver Disease Questionnaire [CLDQ], and Work Productivity and Activity Impairment Questionnaire [WPAI]) to be conducted at baseline/Day 1; Weeks 12, 24, and 48; and the early discontinuation visit (if applicable) for subjects in Cohort C only.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported