Clinical trial results:
A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Multiple Center Study to Evaluate the Safety, Tolerability, and Efficacy of NGM282
Administered for 12 Weeks in Patients with Primary Sclerosing Cholangitis (PSC).

Summary

EudraCT number	2015-003392-30
Trial protocol	GB NL
Global end of trial date	07 June 2017

Results information

Result version number	v1 (current)
This version publication date	15 July 2018
First version publication date	15 July 2018

Trial information

Trial identification

Sponsor protocol code	15-0106

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	NGM Biopharmaceuticals, Inc.
Sponsor organisation address	333 Oyster Point Boulevard, South San Francisco, United States, CA 94080
Public contact	Clinical Operations , NGM Biopharmaceuticals, Inc., 001 6502435555, clinical@ngmbio.com
Scientific contact	Clinical Operations , NGM Biopharmaceuticals, Inc., 001 6502435555, clinical@ngmbio.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	25 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 June 2017
Global end of trial reached?	Yes
Global end of trial date	07 June 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the treatment effect of NGM282 as measured by the mean change in alkaline phosphatase (ALP) from Baseline to Week 12 in patients with Primary Sclerosing Cholangitis (PSC).

Protection of trial subjects:

This study was conducted under the auspices of a data monitoring committee (DMC) to protect subject welfare, preserve study integrity, and provide recommendations as needed regarding study conduct. This study was conducted in compliance with ICH E6 GCP: Consolidated Guidelines pertaining to informed consent.

Background therapy:

Subjects taking medications for IBD (Inflammatory bowel disease - frequently associated with PSC) must have been on a stable regimen of these medications for at least 12 weeks before Day 1 and were to maintain, if possible, a stable dose during the study period.
Subjects taking UDCA (ursodeoxycholic acid) were eligible but must have been on stable doses of <27 mg/kg/day for at least 12 weeks before their screening. No significant dosage changes were to be made during 8 weeks prior to screening and a minimum 8-week washout period was to occur before screening if UDCA was stopped. Subjects not taking UDCA were not to start it during the study period.

Evidence for comparator: -

Actual start date of recruitment	23 February 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	United States: 36
Worldwide total number of subjects	62
EEA total number of subjects	26

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)	57
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects studied had to have confirmed PSC as defined by an elevated ALP and either liver histology or cholangiography consistent with PSC. The presence of IBD was allowed, as well as treatment with a stable regimen of biologic, immunosuppressant, or systemic corticosteroid therapy.

Pre-assignment

Screening details:

A total of 95 subjects were assessed for eligibility after giving informed consent and 62 subjects were randomly assigned to treatment, including 21 subjects
to 1-mg NGM282, 21 subjects to 3-mg NGM282, and 20 subjects to placebo.

Period 1

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

Blinding implementation details:

Syringes containing solutions of NGM282 and placebo were identical in packaging, appearance, and volume of solution. Study drug was coded to preserve blinding.

Arms

Are arms mutually exclusive?	Yes
Arm title	1-mg NGM282

Arm description:

Subjects self-administered study drug (1-mg NGM282, 3-mg NGM282, or matching placebo) as a subcutaneous injection to the abdomen daily, at approximately the same time each morning, over the 12-week treatment period.

Arm type	Experimental
Investigational medicinal product name	NGM282
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

On Day 1 of the study, subjects were trained in study drug administration and were observed self-administering study drug in the clinic by clinic staff. On Weeks 1, 2, 4, 8, and 12, self-administration also occurred in the clinic under observation by clinic staff. All other doses through Week 12 were self-administered at home. Written instructions for study drug preparation and self-administration were provided to each subject and retraining was provided as required at clinic visits.
Subjects were instructed to bring study drug syringes to room temperature before use.
Subjects were required to complete a daily study drug administration diary and return previously dispensed kits of study drug at each clinic visit during the study period after Day 1.

Arm title	3-mg NGM282

Arm description:

Subjects self-administered study drug (1-mg NGM282, 3-mg NGM282, or matching placebo) as a subcutaneous injection to the abdomen daily, at approximately the same time each morning, over the 12-week treatment period.

Arm type	Experimental

Investigational medicinal product name	NGM282
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

On Day 1 of the study, subjects were trained in study drug administration and were observed self-administering study drug in the clinic by clinic staff. On Weeks 1, 2, 4, 8, and 12, self-administration also occurred in the clinic under observation by clinic staff. All other doses through Week 12 were self-administered at home. Written instructions for study drug preparation and self-administration were provided to each subject and retraining was provided as required at clinic visits.
Subjects were instructed to bring study drug syringes to room temperature before use.
Subjects were required to complete a daily study drug administration diary and return previously dispensed kits of study drug at each clinic visit during the study period after Day 1.

Arm title	Placebo

Arm description:

Subjects self-administered study drug (1-mg NGM282, 3-mg NGM282, or matching placebo) as a subcutaneous injection to the abdomen daily, at approximately the same time each morning, over the 12-week treatment period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Study drug was provided as a sterile solution for injection in single-use prefilled syringes for SC administration of 1-mg NGM282, 3-mg NGM282, or placebo.
On Day 1 of the study, subjects were trained in study drug administration and were observed self-administering study drug in the clinic by clinic staff. On Weeks 1, 2, 4, 8, and 12, self-administration also occurred in the clinic under observation by clinic staff. All other doses through Week 12 were self-administered at home. Written instructions for study drug preparation and self-administration were provided to each subject and retraining was provided as required at clinic visits.
Subjects were instructed to bring study drug syringes to room temperature

Number of subjects in period 1	1-mg NGM282	3-mg NGM282	Placebo
Started	21	21	20
Completed	19	18	19
Not completed	2	3	1
Other	-	1	1
Adverse event	1	1	-
Noncompliance with study drug	1	1	-

Baseline characteristics

Reporting groups

Reporting group title	1-mg NGM282

Reporting group description:

Subjects self-administered study drug (1-mg NGM282, 3-mg NGM282, or matching placebo) as a subcutaneous injection to the abdomen daily, at approximately the same time each morning, over the 12-week treatment period.

Reporting group title	3-mg NGM282

Reporting group description:

Subjects self-administered study drug (1-mg NGM282, 3-mg NGM282, or matching placebo) as a subcutaneous injection to the abdomen daily, at approximately the same time each morning, over the 12-week treatment period.

Reporting group title	Placebo

Reporting group description:

Subjects self-administered study drug (1-mg NGM282, 3-mg NGM282, or matching placebo) as a subcutaneous injection to the abdomen daily, at approximately the same time each morning, over the 12-week treatment period.

Reporting group values	1-mg NGM282	3-mg NGM282	Placebo
Number of subjects	21	21	20
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	18	21	19
From 65-84 years	3	0	1
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	7	9	8
Male	14	12	12

Reporting group values	Total		
Number of subjects	62		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	58		
From 65-84 years	4		
85 years and over	0		
Gender categorical Units: Subjects			
Female	24		
Male	38		

Subject analysis sets

Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

Analyses on the per protocol (PP) set were used as a supplement to the FAS analyses and were performed for all efficacy endpoints. The PP set included all subjects in the FAS who had at least 1 valid, non-missing post dose ALP measurement and excluded the following subjects:
- FAS subjects who deviated from the conduct of the study, as adjudicated by the sponsor's medical monitor
- FAS subjects who had an AE deemed by the medical monitor to be impactful on the primary endpoint
In associated analyses, subjects were grouped according to actual treatment received, even if it differed from the assigned treatment.

Subject analysis set title	Full Analysis
Subject analysis set type	Full analysis

Subject analysis set description:

All randomized subjects who received at least 1 dose (full or partial) of study drug and had at least 1 valid, non-missing post dose efficacy parameter value were included in the full analysis set (FAS). This was the set for the primary analyses of efficacy endpoints. In the FAS analyses, subjects were grouped according to the assigned treatment if this differed from the actual treatment received.

Reporting group values	Per Protocol Set	Full Analysis	
Number of subjects	48	62	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	57	44	
From 65-84 years	5	4	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	20	24	
Male	28	38	

End points

End points reporting groups

Reporting group title	1-mg NGM282

Reporting group description:

Subjects self-administered study drug (1-mg NGM282, 3-mg NGM282, or matching placebo) as a subcutaneous injection to the abdomen daily, at approximately the same time each morning, over the 12-week treatment period.

Reporting group title	3-mg NGM282

Reporting group description:

Subjects self-administered study drug (1-mg NGM282, 3-mg NGM282, or matching placebo) as a subcutaneous injection to the abdomen daily, at approximately the same time each morning, over the 12-week treatment period.

Reporting group title	Placebo

Reporting group description:

Subjects self-administered study drug (1-mg NGM282, 3-mg NGM282, or matching placebo) as a subcutaneous injection to the abdomen daily, at approximately the same time each morning, over the 12-week treatment period.

Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

Analyses on the per protocol (PP) set were used as a supplement to the FAS analyses and were performed for all efficacy endpoints. The PP set included all subjects in the FAS who had at least 1 valid, non-missing post dose ALP measurement and excluded the following subjects:
- FAS subjects who deviated from the conduct of the study, as adjudicated by the sponsor’s medical monitor
- FAS subjects who had an AE deemed by the medical monitor to be impactful on the primary endpoint
In associated analyses, subjects were grouped according to actual treatment received, even if it differed from the assigned treatment.

Subject analysis set title	Full Analysis
Subject analysis set type	Full analysis

Subject analysis set description:

All randomized subjects who received at least 1 dose (full or partial) of study drug and had at least 1 valid, non-missing post dose efficacy parameter value were included in the full analysis set (FAS). This was the set for the primary analyses of efficacy endpoints. In the FAS analyses, subjects were grouped according to the assigned treatment if this differed from the actual treatment received.

Primary: The mean change in ALP from Baseline at Week 12

End point title	The mean change in ALP from Baseline at Week 12

End point description:

The primary analysis was performed to evaluate the treatment effect of NGM282. The mean change from Baseline at Week 12 in ALP was compared between each of the 2 active treatment groups (1-mg or 3-mg NGM282) and the placebo group using the Wilcoxon Rank Sum test. Sensitivity analyses for the primary endpoint used a mixed-effect model repeated measures (MMRM) analysis of covariance (ANCOVA).

End point type	Primary

End point timeframe:

The mean change in ALP from Baseline at Week 12 will be compared between each of the two treatment groups (NGM282 1 mg or 3 mg, as applicable) and the placebo group.

End point values	1-mg NGM282	3-mg NGM282	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	21	20	
Units: Mean change in ALP				
number (confidence interval 95%)	21 (-21.1 to 62)	21 (-56 to 26.8)	20 (-38.3 to 48)	

Statistical analyses

Statistical analysis title	SAP, dated 26 May 2017

Statistical analysis description:

Mixed-effect model repeated measures (MMRM) analysis of covariance (ANCOVA) of mean change in ALP from Baseline at Week 12 will be used to compare the difference between treatment groups.
The ANCOVA on the FAS was consistent with the Wilcoxon Rank Sum test and the MMRM analysis.

Comparison groups	1-mg NGM282 v Placebo v 3-mg NGM282
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.511 [2]
Method	ANCOVA/Wilcoxon Rank Sum/MMRM
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.7
upper limit	17.27
Variability estimate	Standard deviation

Notes:

[1] - There was no significant mean percent change from Baseline in ALP in any treatment group at Week 12. There was no significant difference between either the 1-mg or 3-mg dose of NGM282 and placebo, and there was also no significant difference in efficacy between the 1-mg and the 3-mg doses.
[2] - The difference between groups was estimated using the Hodges-Lehmann estimate and confidence interval, and the P-value was computed from the normal approximation of the Wilcoxon Rank Sum test.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

A TEAE was defined as an AE that began on or after the first dose of study drug and before the stop of study drug +30 days.

Adverse event reporting additional description:

A TEAE was defined as an AE that met any of the following conditions:
- Was completely missing a start date and end date
- Was completely missing a start date and the end date was on or after the first dose of study drug

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	1-mg NGM282
Reporting group description: -	
Reporting group title	3-mg NGM282
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	1-mg NGM282	3-mg NGM282	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 21 (4.76%)	2 / 21 (9.52%)	0 / 20 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Bowel obstruction			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Sclerosing cholangitis			

subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Intervertebral discitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	1-mg NGM282	3-mg NGM282	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 21 (80.95%)	20 / 21 (95.24%)	18 / 20 (90.00%)
Cardiac disorders			
ANGINA PECTORIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Nervous system disorders			
BURNING SENSATION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
DIZZINESS			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	2
HEADACHE			
subjects affected / exposed	0 / 21 (0.00%)	4 / 21 (19.05%)	3 / 20 (15.00%)
occurrences (all)	0	4	3
PARAESTHESIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
FATIGUE			

subjects affected / exposed	1 / 21 (4.76%)	3 / 21 (14.29%)	3 / 20 (15.00%)
occurrences (all)	1	3	3
INJECTION SITE ERYTHEMA			
subjects affected / exposed	2 / 21 (9.52%)	11 / 21 (52.38%)	1 / 20 (5.00%)
occurrences (all)	2	11	1
INJECTION SITE PAIN			
subjects affected / exposed	1 / 21 (4.76%)	1 / 21 (4.76%)	2 / 20 (10.00%)
occurrences (all)	1	1	2
MALAISE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
PYREXIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Immune system disorders			
SARCOIDOSIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Eye disorders			
DRY EYE			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
ABDOMINAL CRAMPS			
subjects affected / exposed	1 / 21 (4.76%)	0 / 21 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	2
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
DIARRHEA			
subjects affected / exposed	5 / 21 (23.81%)	4 / 21 (19.05%)	0 / 20 (0.00%)
occurrences (all)	5	4	0
DRY MOUTH			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	0
DYSPEPSIA AGGRAVATED			

subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	0
Frequent bowel movements			
subjects affected / exposed	2 / 21 (9.52%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
INCREASED STOOL FREQUENCY			
subjects affected / exposed	1 / 21 (4.76%)	3 / 21 (14.29%)	0 / 20 (0.00%)
occurrences (all)	1	3	0
LOOSE STOOLS			
subjects affected / exposed	4 / 21 (19.05%)	2 / 21 (9.52%)	1 / 20 (5.00%)
occurrences (all)	4	2	1
NAUSEA			
subjects affected / exposed	2 / 21 (9.52%)	2 / 21 (9.52%)	3 / 20 (15.00%)
occurrences (all)	2	2	3
NAUSEA AGGRAVATED			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
UMBILICAL HERNIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
VOMITING			
subjects affected / exposed	1 / 21 (4.76%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
NASAL CONGESTION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 21 (4.76%)	1 / 21 (4.76%)	2 / 20 (10.00%)
occurrences (all)	1	1	2
Skin and subcutaneous tissue disorders			

PRURITUS			
subjects affected / exposed	1 / 21 (4.76%)	1 / 21 (4.76%)	2 / 20 (10.00%)
occurrences (all)	1	1	2
PRURITUS GENERALISED			
subjects affected / exposed	2 / 21 (9.52%)	2 / 21 (9.52%)	2 / 20 (10.00%)
occurrences (all)	2	2	2
RASH MACULAR			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
SKIN IRRITATION			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
IRRITABILITY			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Infections and infestations			
INFLUENZA			
subjects affected / exposed	0 / 21 (0.00%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
NASOPHARYNGITIS			
subjects affected / exposed	1 / 21 (4.76%)	2 / 21 (9.52%)	4 / 20 (20.00%)
occurrences (all)	1	2	4
RHINITIS			
subjects affected / exposed	0 / 21 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 21 (0.00%)	2 / 21 (9.52%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Metabolism and nutrition disorders			
INCREASED APPETITE			
subjects affected / exposed	4 / 21 (19.05%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	4	1	0
VITAMIN D DEFICIENCY			

subjects affected / exposed occurrences (all)	3 / 21 (14.29%) 3	1 / 21 (4.76%) 1	1 / 20 (5.00%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 November 2015	The following is a summary of the major changes addressed with Protocol Amendment 1, dated 05 Nov 2015: - Calprotectin analysis was added as a study objective, replacing "intestinal inflammatory biomarkers." - Total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides were added as secondary efficacy endpoints. - References to transient elastography were removed. - Various laboratory parameter range inclusion criteria were updated. - The inclusion/exclusion criteria for UDCA use and MRCP findings were updated. - The exclusion criteria were updated to permit subjects to enter the study who were taking antibiotics for the prevention or presumptive treatment of cholangitis and who had compensated cirrhosis. - Clarified that a colonoscopy was to be performed only in subjects with concomitant IBD who did not have a colonoscopy available within 12 months before screening. - Criteria for discontinuation of study treatment for an individual subject were updated, updating threshold levels for ALT, ALP, and total bilirubin. - Additional time points were added for assessment of itch, fatigue, antidrug antibodies, and neutralizing antibodies.
27 May 2016	The following is a summary of the major changes addressed with Protocol Amendment 2, dated 27 May 2016: - "Exploratory markers of fibrogenesis" was added as an exploratory objective. - Inclusion criteria were updated, including the criteria related to the confirmed diagnosis of PSC, carbohydrate antigen 19-9 (CA19-9), UDCA treatment use, concomitant IBD, and platelet levels. - Exclusion criteria were updated, including criteria related to liver disease, MRCP findings, bile duct stenting or drains, acute cholangitis, and decompensated cirrhosis. - Study procedures were updated. - Reporting of local injection-site symptom assessments was clarified. - The interim analysis (IA) procedure was clarified, as was the timing of the EOS visit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported