Clinical trial results:
A Randomised, Double-Blind, Placebo-Controlled Trial of the Safety and Efficacy of Topical Alicaforsen Enema in Subjects with Active, Chronic, Antibiotic Refractory Primary Idiopathic Pouchitis

Summary

EudraCT number	2013-002952-34
Trial protocol	GB NL IE BE IT
Global end of trial date	25 March 2019

Results information

Result version number	v1 (current)
This version publication date	15 February 2020
First version publication date	15 February 2020
Summary attachment (see zip file)	Lay Summary FR (Lay summary _FR.prf.pdf) Lay Summary HE (Lay summary _HE.pdf) Lay Summary IT (Lay summary _IT.pdf) Lay Summary NL (Lay summary _NL.pdf) Lay summary _EN (Lay summary_EN.pdf)

Trial information

Trial identification

Sponsor protocol code	ACH-UCP-301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02525523
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Atlantic Pharmaceuticals Limited
Sponsor organisation address	10 Rose & Crown Walk, Saffron Walden, United Kingdom, CB10 1JH
Public contact	Clinical Development, Atlantic Pharmaceuticals Limited, +44 1 799 513 319, chris@atlantichc.com
Scientific contact	Clinical Development, Atlantic Pharmaceuticals Limited, +44 1 799 513 319, chris@atlantichc.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	31 October 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2018
Global end of trial reached?	Yes
Global end of trial date	25 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the effect of alicaforsen enema on endoscopic healing and symptoms associated with pouchitis in subjects with active pouchitis

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki (October 2013), in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP: CPMP/ICH/135/95; July 1996), and all applicable regulatory requirements in the countries of conduct.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 February 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	United Kingdom: 22
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Ireland: 6
Country: Number of subjects enrolled	Canada: 21
Country: Number of subjects enrolled	Switzerland: 11
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Italy: 26
Country: Number of subjects enrolled	United States: 29
Worldwide total number of subjects	138
EEA total number of subjects	75

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)	131
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Main Study - Subjects provided informed consent and completed a Screening period of up to 3 weeks to provide baseline health status data and to be assessed for eligibility.
Pharmacokinetic Addendum - Subjects provided separate informed consent and completed a 2 week Screening period

Period 1

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

Blinding implementation details:

The placebo enema exactly matched the alicaforsen enema and both were packaged identically. The Investigator was to make every effort to contact the Sponsor before unblinding any subject's treatment assignment and the identity of the treatment group assigned to subjects was to be provided in an emergency only. No subjects were unblinded during the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Alicaforsen Enema (Main study)

Arm description:

Subjects were randomised to alicaforsen enema or placebo enema on the main study.

Arm type	Experimental
Investigational medicinal product name	Alicaforsen
Investigational medicinal product code	
Other name	Alicaforsen sodium
Pharmaceutical forms	Rectal solution
Routes of administration	Rectal use

Dosage and administration details:

Each subject self-administered a 240 mg alicaforsen enema once daily for 42 days (6 weeks) ± 6 days.

Arm title	Placebo Enema (Main study)

Arm description:

Subjects were randomised to alicaforsen enema or placebo enema on the main study.

Arm type	Placebo
Investigational medicinal product name	Placebo Enema
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Rectal solution
Routes of administration	Rectal use

Dosage and administration details:

Each subject self-administered a placebo enema once daily for 42 days (6 weeks) ± 6 days

Number of subjects in period 1	Alicaforsen Enema (Main study)	Placebo Enema (Main study)
Started	69	69
Completed	46	44
Not completed	23	25
Consent withdrawn by subject	11	12
Physician decision	5	5
Adverse event, non-fatal	3	3
Need for rescue medication	1	-
Lack of efficacy - start open label	-	1
Open-label Access	-	1
Discontinuation Criteria Met	-	1
Protocol deviation	2	1
Lack of efficacy	1	1

Period 2

Period 2 title	Open label study
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Alicaforsen enema (Open label)

Arm description:

All subjects received alicaforsen enema on the open label study.

Arm type	Experimental
Investigational medicinal product name	Alicaforsen
Investigational medicinal product code	
Other name	Alicaforsen sodium
Pharmaceutical forms	Rectal solution
Routes of administration	Rectal use

Dosage and administration details:

Each subject self-administered a 240 mg alicaforsen enema for 42 days (6 weeks). 54 subjects had one treatment, 11 subjects had between 2 and 5 treatments.

Number of subjects in period 2[1]	Alicaforsen enema (Open label)
Started	65
Completed	65

Notes:

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

Justification: Following the final Follow-up visit at Week 26, subjects who met the criteria for open label access could decide to continue to receive alicaforsen enema during the open access part of the protocol. Not all subjects who completed the Main Study continued to the open label study.

Period 3

Period 3 title	Pharmacokinetic Addendum
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Alicaforsen Enema (PK addendum)

Arm description:

All subjects received alicaforsen enema on the pharmacokinetic addendum. Additional subjects (up to 6 subjects planned) were recruited at a single site to evaluate the PK of open label alicaforsen.

Arm type	Experimental
Investigational medicinal product name	Alicaforsen
Investigational medicinal product code	
Other name	Alicaforsen sodium
Pharmaceutical forms	Rectal solution
Routes of administration	Rectal use

Dosage and administration details:

Each subject self-administered a 240 mg alicaforsen enema once daily for 42 days (6 weeks).

Number of subjects in period 3[2]	Alicaforsen Enema (PK addendum)
Started	4
Completed	3
Not completed	1
Lost to follow-up	1

Notes:

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

Justification: A total of 6 subjects were planned to be recruited at a single site in the UK to evaluate the PK of open label alicaforsen. The actual number of subjects recruited was 4. These subjects did not take part in the Main Study.

Baseline characteristics

Reporting groups	
Reporting group title	Alicaforsen Enema (Main study)
Reporting group description:	
Subjects were randomised to alicaforsen enema or placebo enema on the main study.	
Reporting group title	Placebo Enema (Main study)
Reporting group description:	
Subjects were randomised to alicaforsen enema or placebo enema on the main study.	

Reporting group values	Alicaforsen Enema (Main study)	Placebo Enema (Main study)	Total
Number of subjects	69	69	138
Age categorical Units: Subjects			
Adults (18-64 years)	65	66	131
From 65-84 years	4	3	7
Gender categorical Units: Subjects			
Female	30	28	58
Male	39	41	80
Ethnic origin Units: Subjects			
Hispanic or Latino	2	1	3
Not Hispanic or Latino	62	62	124
Not Reported	5	6	11
Race Units: Subjects			
Black or African American	1	0	1
American Indian or Alaska Native	0	0	0
Asian	1	5	6
Native Hawaiian or Other Pacific Islander	0	0	0
White	62	54	116
Other	0	4	4
Not Reported	5	6	11
Smoking history Units: Subjects			
Never smoked	51	46	97
Former smoker	15	17	32
Current smoker	3	6	9

End points

End points reporting groups

Reporting group title	Alicaforsen Enema (Main study)
Reporting group description:	
Subjects were randomised to alicaforsen enema or placebo enema on the main study.	
Reporting group title	Placebo Enema (Main study)
Reporting group description:	
Subjects were randomised to alicaforsen enema or placebo enema on the main study.	
Reporting group title	Alicaforsen enema (Open label)
Reporting group description:	
All subjects received alicaforsen enema on the open label study.	
Reporting group title	Alicaforsen Enema (PK addendum)
Reporting group description:	
All subjects received alicaforsen enema on the pharmacokinetic addendum. Additional subjects (up to 6 subjects planned) were recruited at a single site to evaluate the PK of open label alicaforsen.	
Subject analysis set title	Alicaforsen enema (Main Study - Full Analysis Set)
Subject analysis set type	Full analysis
Subject analysis set description:	
The Full Analysis Set included all randomised subjects with confirmed active pouchitis (determined by meeting inclusion criteria 4, 5, 7, and 8 per Section 9.3.1.1) at Baseline, and who received at least 1 dose of study drug and had at least 1 post Baseline assessment of efficacy i.e., subject had at least 7 consecutive days of post Baseline diary data and had at least 4 days of data recorded within those 7 days. This analysis set was used to assess the efficacy endpoints. Following the intent-to-treat principle, subjects were analysed according to the treatment they were assigned to at randomisation, irrespective of the treatment they received.	
Subject analysis set title	Placebo enema (Main Study - Full Analysis Set)
Subject analysis set type	Full analysis
Subject analysis set description:	
The Full Analysis Set included all randomised subjects with confirmed active pouchitis (determined by meeting inclusion criteria 4, 5, 7, and 8 per Section 9.3.1.1) at Baseline, and who received at least 1 dose of study drug and had at least 1 post Baseline assessment of efficacy i.e., subject had at least 7 consecutive days of post Baseline diary data and had at least 4 days of data recorded within those 7 days. This analysis set was used to assess the efficacy endpoints. Following the intent-to-treat principle, subjects were analysed according to the treatment they were assigned to at randomisation, irrespective of the treatment they received.	

Primary: Proportion of Subjects with Endoscopic Remission at Week 10

End point title	Proportion of Subjects with Endoscopic Remission at Week 10
End point description:	
Proportion of subjects with endoscopic remission was defined as absence of friability and ulceration, represented by a score of <1 (endoscopy component of a modified Mayo score). The area within 1 cm of the pouch suture line was not included in the endoscopic evaluation.	
End point type	Primary
End point timeframe:	
Week 10	

End point values	Alicaforsen enema (Main Study - Full Analysis Set)	Placebo enema (Main Study - Full Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	65	61		
Units: Subjects				
Number of subejcts with endoscopic remission	3	3		

Statistical analyses

Statistical analysis title	Adjusted odds ratio
Comparison groups	Alicaforsen enema (Main Study - Full Analysis Set) v Placebo enema (Main Study - Full Analysis Set)
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9363
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.181
upper limit	4.819

Primary: Proportion of Subjects who Achieved a Modified Mayo Stool Frequency Score ≤1 at Week 10

End point title	Proportion of Subjects who Achieved a Modified Mayo Stool Frequency Score ≤1 at Week 10
End point description:	
Proportion of subjects with a stool frequency represented by a modified Mayo subscore of <1	
End point type	Primary
End point timeframe:	
Week 10	

End point values	Alicaforsen enema (Main Study - Full Analysis Set)	Placebo enema (Main Study - Full Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	65	61		
Units: Subjects				
Achieved a Mayo stool frequency ≤ 1	22	16		

Statistical analyses

Statistical analysis title	Adjusted odds ratio
Comparison groups	Alicaforsen enema (Main Study - Full Analysis Set) v Placebo enema (Main Study - Full Analysis Set)
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.355
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.668
upper limit	3.103

Secondary: Percentage Change from Baseline in Stool Frequency at Week 6 and Week 10

End point title	Percentage Change from Baseline in Stool Frequency at Week 6 and Week 10
End point description:	
Percentage change in stool frequency from Baseline compared to placebo	
End point type	Secondary
End point timeframe:	
Week 6 and Week 10	

End point values	Alicaforsen enema (Main Study - Full Analysis Set)	Placebo enema (Main Study - Full Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	65	61		
Units: Percentage change from baseline				
least squares mean (standard error)				
Week 6	-14.61 (± 4.79)	-16.67 (± 5.02)		
Week 10	-14.46 (± 4.79)	-14.61 (± 5.02)		

Statistical analyses

Statistical analysis title	Treatment difference (Week 6)
Comparison groups	Placebo enema (Main Study - Full Analysis Set) v Alicaforsen enema (Main Study - Full Analysis Set)
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5894
Method	ANCOVA
Parameter estimate	Standard error
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.45
upper limit	9.56

Statistical analysis title	Treatment difference (Week 10)
Comparison groups	Alicaforsen enema (Main Study - Full Analysis Set) v Placebo enema (Main Study - Full Analysis Set)
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9677
Method	ANCOVA
Parameter estimate	Standard error
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.35
upper limit	7.66

Secondary: Change from Baseline in Urgency Score at Week 6	
End point title	Change from Baseline in Urgency Score at Week 6
End point description:	
Change in urgency score from Baseline compared to placebo	
End point type	Secondary
End point timeframe:	
Week 6	

End point values	Alicaforsen enema (Main Study - Full Analysis Set)	Placebo enema (Main Study - Full Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	59	58		
Units: Percentage change from baseline				
least squares mean (standard error)	-10.77 (± 4.72)	-15.41 (± 4.80)		

Statistical analyses

Statistical analysis title	Treatment difference
Comparison groups	Alicaforsen enema (Main Study - Full Analysis Set) v Placebo enema (Main Study - Full Analysis Set)
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1944
Method	ANCOVA
Parameter estimate	Standard error
Point estimate	3.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.39
upper limit	11.67

Secondary: Change from Baseline in Rectal Bleeding Score at Week 6

End point title	Change from Baseline in Rectal Bleeding Score at Week 6
End point description:	
Change in rectal bleeding score from Baseline compared to placebo	
End point type	Secondary
End point timeframe:	
Week 6	

End point values	Alicaforsen enema (Main Study - Full Analysis Set)	Placebo enema (Main Study - Full Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	65	60		
Units: Adjusted Odds				
number (confidence interval 95%)	3.91 (0.70 to 21.83)	9.46 (1.57 to 57.03)		

Statistical analyses

Statistical analysis title	Adjusted odds ratio
Comparison groups	Alicaforsen enema (Main Study - Full Analysis Set) v Placebo enema (Main Study - Full Analysis Set)
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0413
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	0.97

Secondary: Proportion of Subjects Who Achieved Total PDAI Score <5 at Both Week 6 and Week 10

End point title	Proportion of Subjects Who Achieved Total PDAI Score <5 at Both Week 6 and Week 10
End point description:	
Proportion of subjects who achieved overall Pouchitis Disease Activity Index (PDAI) <5	
End point type	Secondary
End point timeframe:	
Week 6 and Week 10	

End point values	Alicaforsen enema (Main Study - Full Analysis Set)	Placebo enema (Main Study - Full Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	65	61		
Units: Subjects				
Total PDAI Score <5 at both Week 6 and Week 10	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Cleveland Global Quality of Life at Week 6

End point title	Change from Baseline in Cleveland Global Quality of Life at Week 6

End point description:

End point type	Secondary

End point timeframe:

Week 6

End point values	Alicaforsen enema (Main Study - Full Analysis Set)	Placebo enema (Main Study - Full Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	60		
Units: Change from baseline				
least squares mean (standard error)	0.0723 (± 0.0278)	0.0436 (± 0.0291)		

Statistical analyses

Statistical analysis title	Treatment difference
Comparison groups	Alicaforsen enema (Main Study - Full Analysis Set) v Placebo enema (Main Study - Full Analysis Set)
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2057
Method	ANCOVA
Parameter estimate	Standard error
Point estimate	0.0226
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0159
upper limit	0.0734

Secondary: Proportion of Subjects Who Had Not Received Additional Treatment for Pouchitis Flares by Week 26

End point title	Proportion of Subjects Who Had Not Received Additional Treatment for Pouchitis Flares by Week 26

End point description:

End point type	Secondary

End point timeframe:

Week 26

End point values	Alicaforsen enema (Main Study - Full Analysis Set)	Placebo enema (Main Study - Full Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	65	60		
Units: Adjusted odds				
least squares mean (confidence interval 95%)	2.24 (0.69 to 7.24)	2.33 (0.67 to 8.11)		

Statistical analyses

Statistical analysis title	Adjusted odds ratio
Comparison groups	Alicaforsen enema (Main Study - Full Analysis Set) v Placebo enema (Main Study - Full Analysis Set)
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.921
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	2.1

Secondary: Proportion of subjects who achieved endoscopic response (PK addendum)

End point title	Proportion of subjects who achieved endoscopic response (PK addendum)

End point description:

Proportion of subjects who achieved endoscopic response defined as improvement of >1 point on the endoscopic component of the modified Mayo score, as read by the Investigator.

End point type	Secondary

End point timeframe:

Week 10

End point values	Alicaforsen Enema (PK addendum)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects				
Achieved endoscopic response	2			
Did not achieve endoscopic response	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects who achieved histological response (PK addendum)

End point title	Proportion of subjects who achieved histological response (PK addendum)

End point description:

Histological response was defined as PDAI subscore 1 (for subjects with Baseline score >1) or >2-point reduction from Baseline.

End point type	Secondary

End point timeframe:

Day 73

End point values	Alicaforsen Enema (PK addendum)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects				
Achieved histological response	1			
Did not achieve histological response	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects who achieved histological remission (PK addendum)

End point title	Proportion of subjects who achieved histological remission (PK addendum)

End point description:

Histological remission was defined as PDAI subscore 0for subjects with a Baseline subscore above 0.

End point type	Secondary

End point timeframe:

Day 73

End point values	Alicaforsen Enema (PK addendum)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Subjects				
Achieved histological remission	0			
Did not achieve histological remission	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TEAEs were defined as AEs with an onset date and time on or after the day and time of the first dose of study drug up to 30 days after last dose of study drug. Serious adverse events were reported to the Sponsor within 24 hours of occurring.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Alicaforsen Enema (Safety Analysis set)

Reporting group description:

The safety analysis set includes all subjects who were randomised and received a dose of study drug. This analysis set was used to assess all safety endpoints. Subjects were analysed according to the treatment they received.

Reporting group title	Placebo Enema (Safety Analysis Set)

Reporting group description:

The safety analysis set includes all subjects who were randomised and received a dose of study drug. This analysis set was used to assess all safety endpoints. Subjects were analysed according to the treatment they received.

Reporting group title	Alicaforsen Enema (PK addendum - Safety Analysis Set)

Reporting group description:

The safety analysis set includes all subjects who received a dose of study drug. This analysis set was used to assess all safety endpoints.

Reporting group title	Alicaforsen enema (Open label study)

Reporting group description:

This group includes all subjects who received study drug during the open label study. Serious adverse events only were collected from this group of patients.

Serious adverse events	Alicaforsen Enema (Safety Analysis set)	Placebo Enema (Safety Analysis Set)	Alicaforsen Enema (PK addendum - Safety Analysis Set)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 69 (5.80%)	2 / 68 (2.94%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	1 / 69 (1.45%)	0 / 68 (0.00%)	0 / 4 (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
Nervous system disorders			
Facial paralysis			

subjects affected / exposed	1 / 69 (1.45%)	0 / 68 (0.00%)	0 / 4 (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
Blood and lymphatic system disorders			
Anaemia aggravated			
subjects affected / exposed	0 / 69 (0.00%)	0 / 68 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 69 (1.45%)	0 / 68 (0.00%)	0 / 4 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 69 (0.00%)	1 / 68 (1.47%)	0 / 4 (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
Gastrointestinal obstruction			
subjects affected / exposed	0 / 69 (0.00%)	1 / 68 (1.47%)	0 / 4 (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
Infections and infestations			
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 68 (0.00%)	0 / 4 (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
Anal abscess			
subjects affected / exposed	1 / 69 (1.45%)	0 / 68 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Alicaforsen enema (Open label study)		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 65 (3.08%)		
number of deaths (all causes)	0		

number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Facial paralysis			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia aggravated			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal obstruction			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 65 (1.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anal abscess			

subjects affected / exposed	0 / 65 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Alicaforsen Enema (Safety Analysis set)	Placebo Enema (Safety Analysis Set)	Alicaforsen Enema (PK addendum - Safety Analysis Set)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 69 (42.03%)	40 / 68 (58.82%)	4 / 4 (100.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 69 (4.35%)	1 / 68 (1.47%)	2 / 4 (50.00%)
occurrences (all)	3	1	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 69 (2.90%)	7 / 68 (10.29%)	0 / 4 (0.00%)
occurrences (all)	3	7	0
Pouchitis			
subjects affected / exposed	4 / 69 (5.80%)	5 / 68 (7.35%)	0 / 4 (0.00%)
occurrences (all)	4	6	0
Anorectal discomfort			
subjects affected / exposed	3 / 69 (4.35%)	4 / 68 (5.88%)	0 / 4 (0.00%)
occurrences (all)	3	4	0
Diarrhoea			
subjects affected / exposed	4 / 69 (5.80%)	1 / 68 (1.47%)	0 / 4 (0.00%)
occurrences (all)	5	1	0
Frequent bowel movements			
subjects affected / exposed	0 / 69 (0.00%)	0 / 68 (0.00%)	3 / 4 (75.00%)
occurrences (all)	0	0	3
Anal haemorrhage			
subjects affected / exposed	0 / 69 (0.00%)	1 / 68 (1.47%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Abdominal discomfort			
subjects affected / exposed	2 / 69 (2.90%)	0 / 68 (0.00%)	1 / 4 (25.00%)
occurrences (all)	2	0	1

Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 69 (0.00%)	2 / 68 (2.94%)	1 / 4 (25.00%)
occurrences (all)	0	2	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 69 (8.70%)	3 / 68 (4.41%)	0 / 4 (0.00%)
occurrences (all)	6	4	0

Non-serious adverse events	Alicaforsen enema (Open label study)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 65 (0.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences (all)	0		
Pouchitis			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences (all)	0		
Anorectal discomfort			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences (all)	0		
Frequent bowel movements			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences (all)	0		
Anal haemorrhage			
subjects affected / exposed	0 / 65 (0.00%)		
occurrences (all)	0		
Abdominal discomfort			

subjects affected / exposed occurrences (all)	0 / 65 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	 0 / 65 (0.00%) 0		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 0 / 65 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 February 2016	Protocol Amendment 2.0 clarified that Israel was participating in the study, clarified inclusion and exclusion criteria, updated the co primary endpoint regarding stool frequency to include a modified Mayo subscore classification, added rectal bleeding as a secondary endpoint, and reordered the tertiary endpoints.
19 August 2016	Protocol Amendment 3.0 added the open label access part of the study to the protocol for all regions except France.
01 December 2017	Protocol Amendment 3.2 added the PK Addendum study for one site in the UK only.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported