



Clinical trial results:

Obeticholic acid treatment in patients with bile acid diarrhoea: an open-label, pilot study of mechanisms, safety and symptom response.

Summary

EudraCT number	2011-003777-28
Trial protocol	GB
Global end of trial date	28 February 2014

Results information

Result version number	v1 (current)
This version publication date	06 February 2020
First version publication date	06 February 2020

Trial information

Trial identification

Sponsor protocol code	OBADIAH1
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01585025
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	South Kensington Campus, London, United Kingdom, SW7 2AZ
Public contact	Julian RF Walters, Imperial College London, julian.walters@imperial.ac.uk
Scientific contact	Julian RF Walters, Imperial College London, julian.walters@imperial.ac.uk

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	02 February 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 January 2014
Global end of trial reached?	Yes
Global end of trial date	28 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to define the change over 2 weeks in serum fibroblast growth factor (FGF19) in 3 groups of patients: primary bile acid diarrhoea, secondary bile acid diarrhoea, and a control population of patients with chronic diarrhoea but with normal bile acid retention.

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 April 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 35
Worldwide total number of subjects	35
EEA total number of subjects	35

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)	25
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited between 2012 and 2014 at Gastrointestinal Outpatient Clinics at Hammersmith and Charing Cross Hospitals

Pre-assignment

Screening details:

35 eligible participants enrolled in the study

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Primary Bile acid diarrhoea

Arm description:

Participants with SeHCAT <10% without other causes such as Crohn's disease and/or ileal resection

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

Dosage and administration details:

Day -14 to Day 0 subjects stopped their usual diarrhoeal medication. Day 1 to Day 15 Obeticholic acid 25mg tablet administered to subjects once daily in the morning. Day 16 to day 28 normal diarrhoeal medication may be re-commenced.

Arm title	Secondary Bile acid diarrhoea
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Arm description:

Participants with Crohn's disease or ileal resection

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

Dosage and administration details:

Day -14 to Day 0 subjects stopped their usual diarrhoeal medication. Day 1 to Day 15 Obeticholic acid 25mg tablet administered to subjects once daily in the morning. Day 16 to day 28 normal diarrhoeal medication may be re-commenced.

Arm title	Idiopathic Diarrhoea Controls
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Arm description:

Participants with Chronic diarrhoea with SeHCAT >15% and no Crohn's or ileal resection

Arm type	Active comparator
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Investigational medicinal product name	Obeticholic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Day -14 to Day 0 subjects stopped their usual diarrhoeal medication. Day 1 to Day 15 Obeticholic acid 25mg tablet administered to subjects once daily in the morning. Day 16 to day 28 normal diarrhoeal medication may be re-commenced.

Number of subjects in period 1	Primary Bile acid diarrhoea	Secondary Bile acid diarrhoea	Idiopathic Diarrhoea Controls
Started	10	13	12
Completed	10	10	8
Not completed	0	3	4
Consent withdrawn by subject	-	3	4

Baseline characteristics

Reporting groups

Reporting group title	Primary Bile acid diarrhoea
Reporting group description:	
Participants with SeHCAT <10% without other causes such as Crohn's disease and/or ileal resection	
Reporting group title	Secondary Bile acid diarrhoea
Reporting group description:	
Participants with Crohn's disease or ileal resection	
Reporting group title	Idiopathic Diarrhoea Controls
Reporting group description:	
Participants with Chronic diarrhoea with SeHCAT >15% and no Crohn's or ileal resection	

Reporting group values	Primary Bile acid diarrhoea	Secondary Bile acid diarrhoea	Idiopathic Diarrhoea Controls
Number of subjects	10	13	12
Age categorical			
Units: Subjects			
Age 18-74	10	10	8
Not recorded	0	3	4
Age continuous			
Units: years			
median	47	45	39
full range (min-max)	24 to 74	27 to 75	25 to 68
Gender categorical			
Units: Subjects			
Female	7	7	3
Male	3	3	5
Not recorded	0	3	4

Reporting group values	Total		
Number of subjects	35		
Age categorical			
Units: Subjects			
Age 18-74	28		
Not recorded	7		
Age continuous			
Units: years			
median			
full range (min-max)	-		
Gender categorical			
Units: Subjects			
Female	17		
Male	11		
Not recorded	7		

Subject analysis sets

Subject analysis set title	Primary Bile acid diarrhoea baseline
Subject analysis set type	Full analysis

Subject analysis set description:

Day 0, baseline analyses

Subject analysis set title	Secondary Bile acid diarrhoea baseline
Subject analysis set type	Full analysis

Subject analysis set description:

Day 0, baseline analyses

Subject analysis set title	Idiopathic Diarrhoea Controls baseline
Subject analysis set type	Full analysis

Subject analysis set description:

Day 0, baseline analyses

Reporting group values	Primary Bile acid diarrhoea baseline	Secondary Bile acid diarrhoea baseline	Idiopathic Diarrhoea Controls baseline
Number of subjects	10	10	8
Age categorical Units: Subjects			
Age 18-74	10	10	8
Not recorded	0	3	4
Age continuous Units: years			
median	47	45	39
full range (min-max)	24 to 74	27 to 75	25 to 68
Gender categorical Units: Subjects			
Female	7	7	3
Male	3	3	5
Not recorded	0	3	4

End points

End points reporting groups

Reporting group title	Primary Bile acid diarrhoea
Reporting group description:	
Participants with SeHCAT <10% without other causes such as Crohn's disease and/or ileal resection	
Reporting group title	Secondary Bile acid diarrhoea
Reporting group description:	
Participants with Crohn's disease or ileal resection	
Reporting group title	Idiopathic Diarrhoea Controls
Reporting group description:	
Participants with Chronic diarrhoea with SeHCAT >15% and no Crohn's or ileal resection	
Subject analysis set title	Primary Bile acid diarrhoea baseline
Subject analysis set type	Full analysis
Subject analysis set description:	
Day 0, baseline analyses	
Subject analysis set title	Secondary Bile acid diarrhoea baseline
Subject analysis set type	Full analysis
Subject analysis set description:	
Day 0, baseline analyses	
Subject analysis set title	Idiopathic Diarrhoea Controls baseline
Subject analysis set type	Full analysis
Subject analysis set description:	
Day 0, baseline analyses	

Primary: Changes in Fasting FGF19

End point title	Changes in Fasting FGF19
End point description:	
End point type	Primary
End point timeframe:	
Day 0, day 15	

End point values	Primary Bile acid diarrhoea	Secondary Bile acid diarrhoea	Idiopathic Diarrhoea Controls	Primary Bile acid diarrhoea baseline
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	10	10	8	10
Units: pg/ml				
median (inter-quartile range (Q1-Q3))	237 (116 to 302)	46 (24 to 72)	194 (126 to 344)	133 (102 to 168)

End point values	Secondary Bile acid diarrhoea baseline	Idiopathic Diarrhoea Controls baseline		
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Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	8		
Units: pg/ml				
median (inter-quartile range (Q1-Q3))	32 (24 to 42)	116 (57 to 186)		

Statistical analyses

Statistical analysis title	FGF19 Primary Bile acid
Statistical analysis description: Compared the baseline to treatment	
Comparison groups	Primary Bile acid diarrhoea v Primary Bile acid diarrhoea baseline
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	FGF19 Secondary Bile acid
Statistical analysis description: Compared the baseline to treatment	
Comparison groups	Secondary Bile acid diarrhoea v Secondary Bile acid diarrhoea baseline
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.11
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	FGF19 Idiopathic Diarrhoea Control
Statistical analysis description: Compared the baseline to treatment	
Comparison groups	Idiopathic Diarrhoea Controls v Idiopathic Diarrhoea Controls baseline
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	FGF19 overall
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Statistical analysis description:

Comparison between the groups

Comparison groups	Idiopathic Diarrhoea Controls v Primary Bile acid diarrhoea v Secondary Bile acid diarrhoea v Idiopathic Diarrhoea Controls baseline v Primary Bile acid diarrhoea baseline v Secondary Bile acid diarrhoea baseline
Number of subjects included in analysis	56
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.0004
Method	Kruskal-wallis

Secondary: Changes in 6h Response (AUC) of FGF19 to OCA

End point title	Changes in 6h Response (AUC) of FGF19 to OCA
End point description: Change in dynamic response of FGF19 in 6 hours following OCA administration; at start and end of 15 day OCA test period.	
End point type	Secondary
End point timeframe: Day 0, day 15	

End point values	Primary Bile acid diarrhoea	Secondary Bile acid diarrhoea	Idiopathic Diarrhoea Controls	Primary Bile acid diarrhoea baseline
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	10	10	8	10
Units: pg/ml				
median (inter-quartile range (Q1-Q3))	3825 (2515 to 6129)	457 (316 to 1016)	2099 (1972 to 2341)	3945 (2609 to 4834)

End point values	Secondary Bile acid diarrhoea baseline	Idiopathic Diarrhoea Controls baseline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	8		
Units: pg/ml				
median (inter-quartile range (Q1-Q3))	401 (267 to 1086)	1644 (1247 to 2776)		

Statistical analyses

Statistical analysis title	FGF19 6h response Primary Bile acid
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Statistical analysis description:

Comparison baseline to treatment

Comparison groups	Primary Bile acid diarrhoea v Primary Bile acid diarrhoea baseline
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.72
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	FGF19 6h response Secondary Bile acid
Statistical analysis description: Comparison baseline to treatment	
Comparison groups	Secondary Bile acid diarrhoea v Secondary Bile acid diarrhoea baseline
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.51
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	FGF19 6h response Idiopathic Control
Statistical analysis description: Comparison baseline to treatment	
Comparison groups	Idiopathic Diarrhoea Controls v Idiopathic Diarrhoea Controls baseline
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Overall FGF19 6h response
Statistical analysis description: Comparison between all treatment	
Comparison groups	Idiopathic Diarrhoea Controls v Primary Bile acid diarrhoea v Secondary Bile acid diarrhoea v Idiopathic Diarrhoea Controls baseline v Primary Bile acid diarrhoea baseline v Secondary Bile acid diarrhoea baseline
Number of subjects included in analysis	56
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.13
Method	Kruskal-wallis

Secondary: Changes in Fasting 7α-hydroxy-4-cholesten-3-one (C4)

End point title	Changes in Fasting 7α-hydroxy-4-cholesten-3-one (C4)
End point description: Change in fasting 7α-hydroxy-4-cholesten-3-one before and after 15 day administration of OCA.	
End point type	Secondary
End point timeframe: Day 0, day 15	

End point values	Primary Bile acid diarrhoea	Secondary Bile acid diarrhoea	Idiopathic Diarrhoea Controls	Primary Bile acid diarrhoea baseline
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	10	10	8	10
Units: microgram/L				
median (inter-quartile range (Q1-Q3))	3 (1 to 17)	56 (14 to 122)	1 (1 to 3)	16 (11 to 37)

End point values	Secondary Bile acid diarrhoea baseline	Idiopathic Diarrhoea Controls baseline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	8		
Units: microgram/L				
median (inter-quartile range (Q1-Q3))	104 (48 to 134)	9 (3 to 14)		

Statistical analyses

Statistical analysis title	C4 Primary Bile Acid
Statistical analysis description: Comparison baseline to treatment	
Comparison groups	Primary Bile acid diarrhoea v Primary Bile acid diarrhoea baseline
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	C4 Secondary Bile Acid
Statistical analysis description: Comparison baseline to treatment	
Comparison groups	Secondary Bile acid diarrhoea v Secondary Bile acid diarrhoea

	baseline
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.11
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	C4 Idiopathic control
Statistical analysis description:	
Comparison baseline to treatment	
Comparison groups	Idiopathic Diarrhoea Controls v Idiopathic Diarrhoea Controls baseline
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	C4 Overall
Statistical analysis description:	
Comparison between treatment	
Comparison groups	Idiopathic Diarrhoea Controls v Primary Bile acid diarrhoea v Secondary Bile acid diarrhoea v Idiopathic Diarrhoea Controls baseline v Primary Bile acid diarrhoea baseline v Secondary Bile acid diarrhoea baseline
Number of subjects included in analysis	56
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.001
Method	Kruskal-wallis

Secondary: Changes in Serum Total Bile Acids

End point title	Changes in Serum Total Bile Acids
End point description:	
Dynamic changes of total bile acids over 6 hour period following OCA administration before and after 15 day OCA period.	
End point type	Secondary
End point timeframe:	
Day 0, day 15	

End point values	Primary Bile acid diarrhoea	Secondary Bile acid diarrhoea	Idiopathic Diarrhoea Controls	Primary Bile acid diarrhoea baseline
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	10	10	8	10
Units: micromol/L				
median (inter-quartile range (Q1-Q3))	0.9 (0.9 to 3)	2.5 (1.0 to 4.0)	1.0 (0.9 to 1.8)	1.5 (1.0 to 4.0)

End point values	Secondary Bile acid diarrhoea baseline	Idiopathic Diarrhoea Controls baseline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	8		
Units: micromol/L				
median (inter-quartile range (Q1-Q3))	2.5 (1.0 to 6.0)	1.5 (1.0 to 2.8)		

Statistical analyses

Statistical analysis title	Bile acid Primary Bile acid
Statistical analysis description:	
Comparison between baseline to treatment	
Comparison groups	Primary Bile acid diarrhoea v Primary Bile acid diarrhoea baseline
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Bile acid Secondary Bile acid
Statistical analysis description:	
Comparison between baseline to treatment	
Comparison groups	Secondary Bile acid diarrhoea v Secondary Bile acid diarrhoea baseline
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Bile acid Idiopathic control
Statistical analysis description:	
Comparison between baseline to treatment	

Comparison groups	Idiopathic Diarrhoea Controls v Idiopathic Diarrhoea Controls baseline
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Bile acid Overall
Statistical analysis description: Comparison between treatments	
Comparison groups	Idiopathic Diarrhoea Controls v Primary Bile acid diarrhoea v Secondary Bile acid diarrhoea v Idiopathic Diarrhoea Controls baseline v Primary Bile acid diarrhoea baseline v Secondary Bile acid diarrhoea baseline
Number of subjects included in analysis	56
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.04
Method	Kruskal-wallis

Secondary: Changes in Stool Frequency (weekly number of stools)

End point title	Changes in Stool Frequency (weekly number of stools)
End point description:	
End point type	Secondary
End point timeframe: Week 2, week 4	

End point values	Primary Bile acid diarrhoea	Secondary Bile acid diarrhoea	Idiopathic Diarrhoea Controls	Primary Bile acid diarrhoea baseline
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	10	10	7	10
Units: stools per week				
median (inter-quartile range (Q1-Q3))	14 (9 to 27)	17 (17 to 42)	18 (13 to 19)	23 (11 to 27)

End point values	Secondary Bile acid diarrhoea baseline	Idiopathic Diarrhoea Controls baseline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	7		
Units: stools per week				

median (inter-quartile range (Q1-Q3))	23 (14 to 44)	15 (11 to 17)		
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Statistical analyses

Statistical analysis title	Weekly stool primary bile acid
Statistical analysis description:	
Comparison between baseline to treatment	
Comparison groups	Primary Bile acid diarrhoea v Primary Bile acid diarrhoea baseline
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Weekly stool secondary bile acid
Statistical analysis description:	
Comparison between baseline to treatment	
Comparison groups	Secondary Bile acid diarrhoea v Secondary Bile acid diarrhoea baseline
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.17
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Weekly stool idiopathic control
Statistical analysis description:	
Comparison between baseline to treatment	
Comparison groups	Idiopathic Diarrhoea Controls v Idiopathic Diarrhoea Controls baseline
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.31
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Weekly stool overall
Statistical analysis description:	
Comparison between treatments	

Comparison groups	Idiopathic Diarrhoea Controls v Secondary Bile acid diarrhoea v Primary Bile acid diarrhoea v Idiopathic Diarrhoea Controls baseline v Primary Bile acid diarrhoea baseline v Secondary Bile acid diarrhoea baseline
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12
Method	Wilcoxon (Mann-Whitney)

Secondary: Changes in Mean Stool Form

End point title	Changes in Mean Stool Form
End point description: Change in mean stool form reported per week between week 2 (baseline) and week 4 (week 2 of treatment) using the Bristol Stool Form Scale (range of scores 1 to 7). High scores are a worse outcome (7=liquid stools).	
End point type	Secondary
End point timeframe: week 2, week 4	

End point values	Primary Bile acid diarrhoea	Secondary Bile acid diarrhoea	Idiopathic Diarrhoea Controls	Primary Bile acid diarrhoea baseline
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	10	10	7	10
Units: Score on Bristol scale				
median (inter-quartile range (Q1-Q3))	4.3 (4.0 to 4.8)	5.6 (4.6 to 6.7)	4.9 (4.1 to 5.0)	5.2 (4.5 to 5.6)

End point values	Secondary Bile acid diarrhoea baseline	Idiopathic Diarrhoea Controls baseline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	7		
Units: Score on Bristol scale				
median (inter-quartile range (Q1-Q3))	6.0 (5.3 to 6.9)	4.9 (4.3 to 5.9)		

Statistical analyses

Statistical analysis title	Mean stool form Primary Bile acid
Statistical analysis description: Comparison between baseline to treatment	
Comparison groups	Primary Bile acid diarrhoea v Primary Bile acid diarrhoea baseline

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Mean stool form Secondary Bile acid
Statistical analysis description:	
Comparison between baseline to treatment	
Comparison groups	Secondary Bile acid diarrhoea v Secondary Bile acid diarrhoea baseline
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Mean stool form Idiopathic control
Statistical analysis description:	
Comparison between baseline to treatment	
Comparison groups	Idiopathic Diarrhoea Controls v Idiopathic Diarrhoea Controls baseline
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.74
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Mean stool form overall
Statistical analysis description:	
Comparison between treatments	
Comparison groups	Idiopathic Diarrhoea Controls v Primary Bile acid diarrhoea v Secondary Bile acid diarrhoea v Idiopathic Diarrhoea Controls baseline v Primary Bile acid diarrhoea baseline v Secondary Bile acid diarrhoea baseline
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Kruskal-wallis

Secondary: Change in Stool Index

End point title	Change in Stool Index
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End point description:

Change in index calculated on a weekly basis, between week 2 (baseline) and week 4 (week 2 of treatment).

The index calculated as ([weekly stool frequency x mean Bristol Stool Form Scale score] = Loperamide use [weekly mg x 3]).

Individual scores ranged from 25 to 1095, with higher scores being worse.

End point type	Secondary
End point timeframe:	
week 2, week 4	

End point values	Primary Bile acid diarrhoea	Secondary Bile acid diarrhoea	Idiopathic Diarrhoea Controls	Primary Bile acid diarrhoea baseline
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	10	10	7	10
Units: index score				
median (inter-quartile range (Q1-Q3))	76 (44 to 104)	127 (47 to 321)	83 (65 to 101)	113 (81 to 144)

End point values	Secondary Bile acid diarrhoea baseline	Idiopathic Diarrhoea Controls baseline		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	7		
Units: index score				
median (inter-quartile range (Q1-Q3))	132 (72 to 473)	96 (69 to 100)		

Statistical analyses

Statistical analysis title	Stool index primary bile acid
Statistical analysis description:	
Comparison between baseline to treatment	
Comparison groups	Primary Bile acid diarrhoea v Primary Bile acid diarrhoea baseline
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Stool index secondary bile acid
Statistical analysis description:	
Comparison between baseline to treatment	

Comparison groups	Secondary Bile acid diarrhoea v Secondary Bile acid diarrhoea baseline
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Stool index idiopathic control
Statistical analysis description:	
Comparison between baseline to treatment	
Comparison groups	Idiopathic Diarrhoea Controls v Idiopathic Diarrhoea Controls baseline
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.61
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Stool index overall
Statistical analysis description:	
Comparison between treatments	
Comparison groups	Idiopathic Diarrhoea Controls v Primary Bile acid diarrhoea v Secondary Bile acid diarrhoea v Idiopathic Diarrhoea Controls baseline v Primary Bile acid diarrhoea baseline v Secondary Bile acid diarrhoea baseline
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0007
Method	Kruskal-wallis

Adverse events

Adverse events information

Timeframe for reporting adverse events:

6 weeks

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	10
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Reporting groups

Reporting group title	Primary Bile acid diarrhoea
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Reporting group description:

Participants with SeHCAT <10% without other causes such as Crohn's disease and/or ileal resection

Reporting group title	Secondary Bile acid diarrhoea
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Reporting group description:

Participants with Crohn's disease or ileal resection

Reporting group title	Idiopathic Diarrhoea Controls
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Reporting group description:

Participants with Chronic diarrhoea with SeHCAT >15% and no Crohn's or ileal resection

Serious adverse events	Primary Bile acid diarrhoea	Secondary Bile acid diarrhoea	Idiopathic Diarrhoea Controls
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Primary Bile acid diarrhoea	Secondary Bile acid diarrhoea	Idiopathic Diarrhoea Controls
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	1 / 8 (12.50%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Gastrointestinal disorders			
Constipation/abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Recruitment in the idiopathic chronic diarrhoea control group did not reach the prespecified number of 10 due to dropouts. Of the 8 subjects recruited, one failed to return diaries that could be analyzed.
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Notes: