Clinical trial results:
A once weekly, repeated dose, placebo controlled, double blind, randomised cross-over trial investigating safety, efficacy and pharmacodynamics of FE 203799 in patients with short bowel syndrome with intestinal failure requiring parenteral support followed by an additional treatment period in an open label regimen.

Summary

EudraCT number	2017-002486-21
Trial protocol	DK
Global end of trial date	21 November 2019

Results information

Result version number	v1 (current)
This version publication date	06 January 2021
First version publication date	06 January 2021

Trial information

Trial identification

Sponsor protocol code	GLY-311-2017

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GLyPharma Therapeutic Inc.
Sponsor organisation address	1188 Avenue Union, Suite 504/505, Montreal, Canada, H3B 0E5
Public contact	Christian Meyer, GLyPharma Therapeutic, Inc. (a wholly owned subsidiary of VectivBio Holding AG), 0041 796543455, christian.meyer@vectivbio.com
Scientific contact	Christian Meyer, GLyPharma Therapeutic, Inc. (a wholly owned subsidiary of VectivBio Holding AG), 0041 796543455, christian.meyer@vectivbio.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	07 April 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 November 2019
Global end of trial reached?	Yes
Global end of trial date	21 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of FE 203799 in patients with short bowel syndrome (SBS) with intestinal failure.

Protection of trial subjects:

This trial was conducted in accordance with the ICH GCP guidelines, including the archiving of essential documents, and with the ethical principles that have their origin in the Declaration of Helsinki. Personal data included in the clinical trial report were collected and processed in accordance with the EU General Data Protection Regulation.

Background therapy:

Parenteral support ≥3 times/week for ≥12 months according to the patient’s medical record.

Evidence for comparator:

FE 203799 was compared to placebo.

Actual start date of recruitment	08 May 2018
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	Denmark: 8
Worldwide total number of subjects	8
EEA total number of subjects	8

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)	5
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The subjects were recruited at a single trial centre in Denmark.

Pre-assignment

Screening details:

A total of 12 subjects were screened and 8 were randomised in the trial. The reasons for the screen failures were inadequate hepatic or renal function for 3 subjects, while the fourth screen failure subject was not considered eligible due to catheter sepsis, which occurred after the screening visit.

Period 1

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

Blinding implementation details:

To minimise bias, part A of this trial was designed as a placebo controlled, double blind, randomised trial. Furthermore, since SBS is characterised by large heterogeneity, a cross-over design, where each patient acted as his/her own control in the analysis of the trial results, was chosen to minimise variation.

Arms

Are arms mutually exclusive?	Yes
Arm title	FE 203799 crossover to placebo

Arm description:

Repeated dose treatment with FE 203799 followed by cross-over to repeated dose treatment with placebo.

Arm type	Experimental
Investigational medicinal product name	FE 203799
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The subjects were to receive a subcutaneous dose of 5 mg FE 203799 once weekly for 4 weeks followed by a washout period of 6-10 weeks. The subjects crossed-over to receive subcutaneous placebo once weekly for 4 weeks followed by a washout period of 6-10 weeks.

Arm title	Placebo crossover to FE 203799

Arm description:

Repeated dose treatment with placebo followed by cross-over to repeated dose treatment with FE 203799.

Arm type	Experimental
Investigational medicinal product name	FE 203799
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The subjects were to receive subcutaneous placebo once weekly for 4 weeks followed by a washout period of 6-10 weeks. The subjects crossed-over to receive a subcutaneous dose of 5 mg FE 203799 once weekly for 4 weeks followed by a washout period of 6-10 weeks.

Number of subjects in period 1	FE 203799 crossover to placebo	Placebo crossover to FE 203799
Started	4	4
Completed	4	4

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

Blinding implementation details:

Not blinded.

Arms

Arm title	FE 203799 open-label extension

Arm description:

Repeated dose treatment with FE 203799.

Arm type	Experimental
Investigational medicinal product name	FE 203799
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The subjects were to receive a subcutaneous dose of 10 mg FE 203799 once weekly for 4 weeks.

Number of subjects in period 2	FE 203799 open-label extension
Started	8
Completed	7
Not completed	1
Subject wishes to terminate	1

Baseline characteristics

Reporting groups	
Reporting group title	FE 203799 crossover to placebo
Reporting group description:	
Repeated dose treatment with FE 203799 followed by cross-over to repeated dose treatment with placebo.	
Reporting group title	Placebo crossover to FE 203799
Reporting group description:	
Repeated dose treatment with placebo followed by cross-over to repeated dose treatment with FE 203799.	

Reporting group values	FE 203799 crossover to placebo	Placebo crossover to FE 203799	Total
Number of subjects	4	4	8
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)	2	3	5
From 65-84 years	2	1	3
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	57.30	61.00	
standard deviation	± 18.50	± 9.70	-
Gender categorical			
Units: Subjects			
Female	1	3	4
Male	3	1	4
Race			
Units: Subjects			
white	4	4	8
Weight			
Units: kg			
arithmetic mean	77.20	74.00	
standard deviation	± 17.30	± 15.90	-
BMI			
Units: kg/m2			
arithmetic mean	24.60	25.10	
standard deviation	± 3.70	± 4.60	-

Subject analysis sets	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
Full analysis set	
Subject analysis set title	FE 203799 5 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients who had received FE 203799 5 mg in either arm.	
Subject analysis set title	FE 203799 10 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients who had received FE 203799 10 mg in either arm.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients who had received placebo in either arm.	

Reporting group values	Full analysis set	FE 203799 5 mg	FE 203799 10 mg
Number of subjects	8	8	8
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	5		
From 65-84 years	3		
85 years and over			
Age continuous			
Units: years			
arithmetic mean	59.10		
standard deviation	± 13.80	±	±
Gender categorical			
Units: Subjects			
Female	4		
Male	4		
Race			
Units: Subjects			
white	8		
Weight			
Units: kg			
arithmetic mean	75.60		
standard deviation	± 15.50	±	±
BMI			
Units: kg/m2			
arithmetic mean	24.80		
standard deviation	± 3.90	±	±

Reporting group values	Placebo		
Number of subjects	8		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years arithmetic mean standard deviation	±		
Gender categorical Units: Subjects			
Female Male			
Race Units: Subjects			
white			
Weight Units: kg arithmetic mean standard deviation	±		
BMI Units: kg/m2 arithmetic mean standard deviation	±		

End points

End points reporting groups

Reporting group title	FE 203799 crossover to placebo
Reporting group description:	
Repeated dose treatment with FE 203799 followed by cross-over to repeated dose treatment with placebo.	
Reporting group title	Placebo crossover to FE 203799
Reporting group description:	
Repeated dose treatment with placebo followed by cross-over to repeated dose treatment with FE 203799.	
Reporting group title	FE 203799 open-label extension
Reporting group description:	
Repeated dose treatment with FE 203799.	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
Full analysis set	
Subject analysis set title	FE 203799 5 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients who had received FE 203799 5 mg in either arm.	
Subject analysis set title	FE 203799 10 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients who had received FE 203799 10 mg in either arm.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients who had received placebo in either arm.	

Primary: Adverse events

End point title	Adverse events[1]
End point description:	
Number of subjects with adverse events.	
End point type	Primary
End point timeframe:	
Treatment emergent adverse events were defined as those with onset on or after the day of the first IMP administration until the end-of-trial visit.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical comparisons of adverse event incidence rates between the reporting groups were performed.

End point values	FE 203799 5 mg	FE 203799 10 mg	Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	8	8	
Units: Subjects	8	8	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in urinary output

End point title	Absolute change in urinary output

End point description:

Absolute change in urinary output from baseline to end of treatment.

End point type	Secondary

End point timeframe:

From baseline to the end of the treatment period.

End point values	FE 203799 5 mg	FE 203799 10 mg	Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	7	8	
Units: mL/day				
arithmetic mean (standard deviation)	545.2 (± 484.8)	629.7 (± 640.4)	-185.5 (± 289.7)	

Statistical analyses

Statistical analysis title	Absolute change from baseline in urinary output

Statistical analysis description:

Absolute changes from baseline to end of treatment for the full population of 8 subjects was derived using a linear mixed-effects analysis of covariance (ANCOVA) model and the corresponding mean value together with the 95% confidence interval. The 8 subjects were tested in a cross-over design, resulting in 23 observations.

Comparison groups	FE 203799 5 mg v Placebo
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0209
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	710.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	132.4
upper limit	1289.39

Statistical analysis title	Absolute change from baseline in urinary output

Statistical analysis description:

Absolute changes from baseline to end of treatment for the full population of 8 subjects was derived using a linear mixed-effects analysis of covariance (ANCOVA) model and the corresponding mean value together with the 95% confidence interval. The 8 subjects were tested in a cross-over design, resulting in 23 observations.

Comparison groups	FE 203799 10 mg v Placebo
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0144
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	794.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	195.31
upper limit	1394.29

Statistical analysis title	Absolute change from baseline in urinary output

Statistical analysis description:

Absolute changes from baseline to end of treatment for the full population of 8 subjects was derived using a linear mixed-effects analysis of covariance (ANCOVA) model and the corresponding mean value together with the 95% confidence interval. The 8 subjects were tested in a cross-over design, resulting in 23 observations.

Comparison groups	FE 203799 5 mg v FE 203799 10 mg
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.761
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	83.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-514.18
upper limit	681.99

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AE) s were recorded from screening until the final visit 4-6 weeks after the last dose.

Adverse event reporting additional description:

An AE having onset on or after the day of the first administration of trial drug was considered treatment emergent. Adverse events were reported for the safety analysis set, comprising all subjects who received a treatment injection at least once.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	FE 203799 5 mg

Reporting group description:

All patients who had received FE 203799 5 mg in either arm.

Reporting group title	FE 203799 10 mg

Reporting group description:

All patients who had received FE 203799 10 mg in either arm.

Reporting group title	Placebo

Reporting group description:

All patients who had received placebo in either arm.

Serious adverse events	FE 203799 5 mg	FE 203799 10 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	2 / 8 (25.00%)	3 / 8 (37.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Complication associated with device			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (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			
Device related sepsis			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	2 / 8 (25.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device occlusion			

subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (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
Device damage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	FE 203799 5 mg	FE 203799 10 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	8 / 8 (100.00%)	8 / 8 (100.00%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Oedema			
subjects affected / exposed	2 / 8 (25.00%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	8	4	0
Injection site erythema			
subjects affected / exposed	1 / 8 (12.50%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	2	5	0
Thirst decreased			
subjects affected / exposed	3 / 8 (37.50%)	4 / 8 (50.00%)	0 / 8 (0.00%)
occurrences (all)	3	4	0
Injection site pruritus			
subjects affected / exposed	1 / 8 (12.50%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	1	4	0
Fatigue			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Catheter site erythema			

subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Oedema peripheral			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Early satiety			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Drug effect decreased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Investigations			
Gastrointestinal stoma output abnormal			
subjects affected / exposed	4 / 8 (50.00%)	4 / 8 (50.00%)	0 / 8 (0.00%)
occurrences (all)	7	5	0
Gastrointestinal stoma output decreased			
subjects affected / exposed	3 / 8 (37.50%)	6 / 8 (75.00%)	0 / 8 (0.00%)
occurrences (all)	3	6	0
Weight increased			
subjects affected / exposed	1 / 8 (12.50%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	1	3	0
International normalised ratio increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	3
C-reactive protein increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Carbon dioxide abnormal			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Weight decreased			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Blood urine present			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Stoma complication			
subjects affected / exposed	6 / 8 (75.00%)	6 / 8 (75.00%)	0 / 8 (0.00%)
occurrences (all)	8	9	0
Gastrointestinal stoma complication			
subjects affected / exposed	5 / 8 (62.50%)	5 / 8 (62.50%)	0 / 8 (0.00%)
occurrences (all)	5	5	0
Stoma site erythema			
subjects affected / exposed	0 / 8 (0.00%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Nephrogenic anaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Eye disorders			
Iridocyclitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Frequent bowel movements			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Oral pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Polyuria			
subjects affected / exposed	4 / 8 (50.00%)	6 / 8 (75.00%)	1 / 8 (12.50%)
occurrences (all)	4	6	1
Nephropathy			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Urine odour abnormal			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Oliguria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Micturition urgency			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Acute kidney injury			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			

Limb discomfort			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Device related sepsis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Catheter site infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Bacteraemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	2
Decreased appetite			
subjects affected / exposed	1 / 8 (12.50%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
Hypokalaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Hyperkalaemia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Appetite disorder			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 April 2018	The dose was reduced from 25 mg to 5 mg for the cross-over trial (equal to part A, introduced in amendment 2), to change the approach for the first dosing in patients to a lower dose, which would be optimal for a first-in-patient study, avoiding exposure of patients to potentially unnecessary elevated concentrations of the active compound. The change was based on thorough analyses of older and recent pharmacology data collected in preclinical studies which suggested that a lower dose of FE 203799, such as 5 mg, could also show pharmacological activity.
28 August 2018	The trial was extended from the initial part A (randomised, double-blind, 2-period cross-over) to also include the open label, dose ranging part B in order to enable dose exploration of FE 203799 beyond 5 mg once weekly. Due to the PK/PD profile of FE 203799 (with a half-life of 30 hours) early exploration of dose ranging was justified to adequately determine the risk/benefit of the future recommended dose and/or dose regimen (once weekly and/or every second week) and to guide the dose rationale for future pivotal clinical trials in the SBS population. The introduction of a part B enabled continued open label dose exploration of FE 203799 within the acceptable dose range defined by the no observed adverse effect level (NOAEL) derived from the toxicology studies (rats and minipigs exposed up to 13 weeks) and the phase 1 trials. It was defined that the sponsor's decision on dose escalation to 10 mg or de-escalation to 2.5 mg in part B of the trial would be based on a recommendation from the DMC after review of safety data from a minimum of 4 patients from this trial or another trial actively recruiting patients with SBS (protocol GLY-321-2017). The title of the trial, the trial design figure, the schedule of procedures, and the text in relevant sections of the protocol were updated to describe a third treatment period to test a single dose of FE 203799, which was to be identical to treatment period 1 and 2 and to take place following a 6 to 10 week washout period after the last dose in treatment period 2. The statistical section was updated to include how to analyse data from part B. It was stated that parts A and B of the trial were to be analysed and reported separately.
22 November 2018	The possibility to conduct interim analyses during the trial, if deemed necessary by the sponsor, was introduced. It was stated that any potential influence of interim analysis on the continued study conduct would be minimised by appropriate measures. The sponsor of the trial was changed from GLyPharma Therapeutic Inc. to GLyPharma Therapeutic Inc. (a wholly owned subsidiary of Therachon AG, Aeschenvorstadt 36, CH-4051 Basel Switzerland). Consequently, the sponsor medical officer and list of trial personnel were changed. An additional laboratory was included in order to analyse all exploratory biomarkers. It was clarified that safety case reports would be made accessible to specified, potentially unblinded sponsor personnel, who in case of being unblinded would not take any part in the operational activities. Clarifications related to the introduction of part B in protocol amendment 2 were made to the text. It was deleted that parts A and B of the trial were to be analysed separately.

07 March 2019	Inclusion criterion number 9 was added, stating that male patients had to use barrier contraception during the trial and for 2 weeks after the end-of-trial visit. By error, an inclusion criterion for male contraception had not been included in the original protocol, although it had been included in the patient information sheet and male patients had been informed about thus requirement from the start. Exclusion criterion number 17 was changed so that only patients with changes in the listed treatments within 3 months of screening were to be excluded from the protocol. The original protocol stated that patients using systemic corticosteroids, methotrexate, cyclosporine, tacrolimus, sirolimus, infliximab, or other biologic therapy/immune modifiers within 30 days of screening were to be excluded from the protocol. A common cause of SBS is intestinal resection due to IBD, and consequently SBS patients may receive systemic immune modifiers as IBD treatment. Recent changes in these medications could indicate active disease, while patients that have been on stable treatment for at least 3 months were considered stable and could therefore be included in the protocol. Replacement of patients was changed so that patients not completing part B would also be replaced, so that 8 patients should complete part B. An inconsistency around the wording about FSH testing was addressed so that it was clear that the FSH test should only be used where there was doubt about the patient's menopausal status.
27 June 2019	A change in the company that owns the sponsor, GLyPharma Therapeutic Inc., from Therachon AG to VectivBio Holding AG. A change of company name of one of the analysis laboratories.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported