Clinical trial results:
A Single-Center Phase 3b Trial Investigating the Long-term Effect on Intestinal Absorption, Nutritional Status and Long-Term Safety of treatment with Glepaglutide in Patients with Short Bowel Syndrome (SBS)

Summary

EudraCT number	2020-005194-27
Trial protocol	DK
Global end of trial date	05 September 2023

Results information

Result version number	v1 (current)
This version publication date	12 October 2024
First version publication date	12 October 2024

Trial information

Trial identification

Sponsor protocol code	ZP1848-20060

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1260-2961
Other trial identifiers	IND: 133151

Notes:

Sponsors

Sponsor organisation name	Zealand Pharma A/S
Sponsor organisation address	Sydmarken 11, Søborg, Denmark, DK-2860
Public contact	Head of clinical operations, Zealand Pharma A/S, +45 8877 3600, info@zealandpharma.com
Scientific contact	Head of clinical operations, Zealand Pharma A/S, +45 8877 3600, info@zealandpharma.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	02 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the 24-week effect of glepaglutide on the absorption of fluids.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki, and in adherence to requirements of Good Clinical Practice (GCP) as defined by the International Conference on Harmonization (ICH) Harmonised Tripartite Guideline for Good Clinical Practice.
Before a patient was enrolled into the trial, the patient was informed orally and in writing about the trial by the investigator, and written informed consent was obtained from the patient according to regulatory and legal requirements.
Informed consent of the patient, and the signature of the investigator obtaining the informed consent, were attained before any trial related procedures were performed.

Background therapy:

Medications commonly used to treat SBS symptoms including anti-diarrheal agents were allowed during trial participation; however, changes had to be kept to a minimum and the Medical Monitor to be informed on the reason for the change.
Any medication or vaccine (including over-the-counter or prescription medicines, vitamins, and/or herbal supplements) other than the trial product that the patient had taken within 7 days prior to and including the screening visit, or received during the trial were recorded.

Evidence for comparator:

Not applicable

Actual start date of recruitment	10 August 2021
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	Denmark: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	7
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was planned to enroll a minimum of 6 and a maximum of 16 patients with SBS intestinal failure (SBS-IF) or SBS intestinal insufficiency (SBS-II). All were adults with stable SBS, stable body weight; wet weight of fecal excretion >= 1.500 g/day.

Pre-assignment

Screening details:

A total of 12 patients were screened: 1 patient failed the screening, 1 patient was diagnosed with metastatic colorectal cancer and withdrawn before receiving investigational product.

Period 1

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

Blinding implementation details:

This as an open-label study.

Arms

Arm title	Glepaglutide 10 mg treatment arm

Arm description:

Trial patients received glepaglutide 10 mg once weekly for 52 weeks, with a subsequent 4-week follow-up period.

Arm type	Experimental
Investigational medicinal product name	Glepaglutide 20 mg/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The trial product Glepaglutide 20 mg/mL was administered with single-use autoinjectors as a SC injection with at a dose of 10 mg once weekly for 52 weeks. Patients chose their preferred injection site area- either on their abdomen or their thigh(s). Unless otherwise agreed with the Investigator, patients used this selected injection site area during the entire trial.

Number of subjects in period 1	Glepaglutide 10 mg treatment arm
Started	10
Completed	9
Not completed	1
Fatal Metastatic neoplasm	1

Baseline characteristics

Reporting groups	
Reporting group title	Treatment period

Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	10	10	
Age categorical Units: Subjects			
Adults (18-64 years)	7	7	
From 65-84 years	3	3	
Age continuous Units: years			
arithmetic mean	54.6		
standard deviation	± 15.85	-	
Gender categorical Units: Subjects			
Female	5	5	
Male	5	5	

End points

End points reporting groups

Reporting group title	Glepaglutide 10 mg treatment arm
Reporting group description: Trial patients received glepaglutide 10 mg once weekly for 52 weeks, with a subsequent 4-week follow-up period.	
Subject analysis set title	Baseline group
Subject analysis set type	Full analysis
Subject analysis set description: Participants assessed at Baseline visit.	
Subject analysis set title	24 Week group
Subject analysis set type	Full analysis
Subject analysis set description: Participants assessed at Week 24 visit.	

Primary: Change in absorption of wet weight/fluids from baseline to Week 24

End point title	Change in absorption of wet weight/fluids from baseline to Week 24
End point description: The variable was 24-week change in absorption of wet weight/fluids, the population level summary was the arithmetic mean, and intercurrent events were handled as follows: with regards to intercurrent events like lack of compliance with intake of trial product, lack of compliance with instructions concerning intake of food, fluids or PS, or use of prohibited concomitant medication, the treatment policy strategy was applied, i.e., data were included in the analysis even if collected after occurrence of such an intercurrent event.	
End point type	Primary
End point timeframe: From Baseline to Week 24	

End point values	Baseline group	24 Week group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10[1]		
Units: g/day				
arithmetic mean (standard deviation)				
Absorption of wet weight/fluids (g/day)	841.6 (± 1839.10)	1240.0 (± 1529.74)		

Notes:

[1] - The same subjects analyzed at Baseline.

Statistical analyses

Statistical analysis title	Change in absorption
Comparison groups	24 Week group v Baseline group

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0585
Method	Paired t-test (2-sided, alpha=0.05)
Parameter estimate	Mean difference (final values)
Point estimate	398.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.6
upper limit	814.4
Variability estimate	Standard deviation
Dispersion value	581.6

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Safety data cover the period since the first administrated dose till Week 56.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Treatment arm
Reporting group description:	
Trial patients received glepaglutide 10 mg once weekly for 52 weeks, with a subsequent 4-week follow-up period.	

Serious adverse events	Treatment arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 10 (60.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic neoplasm			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Injury, poisoning and procedural complications			
Stoma obstruction			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Crohn's disease			

subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic fluid collection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pulmonary mass				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Device related sepsis				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Stoma site abscess				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Treatment arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Hypotension			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Vasculitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	7 / 10 (70.00%)		
occurrences (all)	129		
Injection site reaction			
subjects affected / exposed	5 / 10 (50.00%)		
occurrences (all)	19		
Oedema peripheral			
subjects affected / exposed	5 / 10 (50.00%)		
occurrences (all)	6		
Injection site pruritus			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	26		
Fatigue			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Injection site erythema			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	22		
Influenza like illness			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Malaise			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Thirst			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Investigations			
Weight decreased			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Gastrointestinal stoma output abnormal			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Urine output decreased			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Weight increased			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Alanine aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Blood creatinine increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Gastrointestinal stoma output increased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Injury, poisoning and procedural complications Gastrointestinal stoma complication subjects affected / exposed occurrences (all)	8 / 10 (80.00%) 10		
Fall subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Cardiac disorders Supraventricular extrasystoles subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Insomnia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	3 / 10 (30.00%) 3		
Post viral fatigue syndrome subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Ear and labyrinth disorders Hypoacusis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Vertigo			

subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Abdominal distension subjects affected / exposed occurrences (all) Abdominal hernia subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Stomal hernia subjects affected / exposed occurrences (all)	 3 / 10 (30.00%) 4 3 / 10 (30.00%) 3 2 / 10 (20.00%) 2 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1		
Skin and subcutaneous tissue disorders Stoma site dermatitis subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	 2 / 10 (20.00%) 2 1 / 10 (10.00%) 1		
Renal and urinary disorders Nephrolithiasis subjects affected / exposed occurrences (all)	 1 / 10 (10.00%) 1		
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Muscle spasms			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Musculoskeletal discomfort			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Osteoarthritis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Torticollis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	7		
COVID-19			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	3		
Catheter site infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Conjunctivitis			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Erysipelas			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Folliculitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Oesophageal candidiasis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Oral candidiasis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Tooth abscess			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	4		
Decreased appetite			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Hypertriglyceridaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

Hypophosphataemia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 February 2021	Protocol v.2.0 • Exclusion criteria 13 taken out of CSP • Update of Figure 1 • Minor text adjustment • Section 7.2 Patient withdrawal; stressed on importance of FU assessments
02 July 2021	Protocol v.3.0 • Correction of hyperlink, Insertion of new references • Adjustment of PS • New wording of carcinogenic findings and other Adverse Events • Updated wording on clinical safety laboratory assessment • Update of flowchart • Introduction of new endpoint; changes in HbA1c before and after glepaglutide treatment, update of flowchart • Table 11, removal of osmolarity by dipstick

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported