# 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<br>Units: Subjects | | | |
| Adults (18-64 years) | 7 | 7 | |
| From 65-84 years | 3 | 3 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 54.6 | | |
| standard deviation | ± 15.85 | - | |
| Gender categorical<br>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<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | |
| Gastrointestinal stoma output increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | |
| Injury, poisoning and procedural complications<br>Gastrointestinal stoma complication<br>subjects affected / exposed<br>occurrences (all) | 8 / 10 (80.00%)<br>10 | | |
| Fall<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | |
| Cardiac disorders<br>Supraventricular extrasystoles<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | |
| Insomnia<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all) | 3 / 10 (30.00%)<br>3 | | |
| Post viral fatigue syndrome<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | |
| Ear and labyrinth disorders<br>Hypoacusis<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | |
| Vertigo | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | | |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal distension<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal hernia<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)<br><br>Dyspepsia<br>subjects affected / exposed<br>occurrences (all)<br><br>Stomal hernia<br>subjects affected / exposed<br>occurrences (all) | <br><br>3 / 10 (30.00%)<br>4<br><br><br>3 / 10 (30.00%)<br>3<br><br><br>2 / 10 (20.00%)<br>2<br><br><br>1 / 10 (10.00%)<br>1<br><br><br>1 / 10 (10.00%)<br>1<br><br><br>1 / 10 (10.00%)<br>1<br><br><br>1 / 10 (10.00%)<br>1 | | |
| Skin and subcutaneous tissue disorders<br>Stoma site dermatitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Pruritus<br>subjects affected / exposed<br>occurrences (all) | <br><br>2 / 10 (20.00%)<br>2<br><br><br>1 / 10 (10.00%)<br>1 | | |
| Renal and urinary disorders<br>Nephrolithiasis<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 10 (10.00%)<br>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<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>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<br>• Exclusion criteria 13 taken out of CSP<br>• Update of Figure 1<br>• Minor text adjustment<br>• Section 7.2 Patient withdrawal; stressed on importance of FU assessments |
| 02 July 2021 | Protocol v.3.0<br>• Correction of hyperlink, Insertion of new references<br>• Adjustment of PS<br>• New wording of carcinogenic findings and other Adverse Events<br>• Updated wording on clinical safety laboratory assessment<br>• Update of flowchart<br>• Introduction of new endpoint; changes in HbA1c before and after glepaglutide treatment, update of flowchart<br>• Table 11, removal of osmolarity by dipstick |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported