# Clinical trial results:
# enliGHten: A Multicenter, Phase 3, Long-term, Open-label Trial Investigating Safety and Efficacy of TransCon hGH Administered Once-Weekly in Children with Growth Hormone Deficiency (GHD) Who Have Completed a Prior Lonapegsomatropin Clinical Trial

## Summary

| | |
|---|---|
| EudraCT number | 2017-003410-20 |
| Trial protocol | BG GR IT PL RO |
| Global end of trial date | 15 August 2023 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 21 December 2023 |
| First version publication date | 21 December 2023 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | TransCon_hGH_CT-301EXT |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03344458 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Ascendis Pharma Endocrinology Division A/S |
| Sponsor organisation address | Tuborg Boulevard 12, Hellerup, Denmark, 2900 |
| Public contact | Clinical Trial Information Desk, Ascendis Pharma A/S, 0045 70222244, clinhelpdesk@ascendispharma.com |
| Scientific contact | Clinical Trial Information Desk, Ascendis Pharma A/S, 0045 70222244, clinhelpdesk@ascendispharma.com |

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-002692-PIP01-19 |
| 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? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 15 August 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 22 February 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 15 August 2023 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To assess long-term safety of weekly lonapegsomatropin hGH in children with GHD previously treated in a phase 3 TransCon hGH trial.

Protection of trial subjects:

Independent safety committee provided independent oversight of the trial participants, by reviewing the progress of the trial and by assessing the accumulated safety data.
It was anticipated based on previous trials that the safety and efficacy profile is comparable to currently approved daily hGH products while maintaining exposure in the optimal therapeutic range. The safety and efficacy of the patients were regularly monitored during the study conduct, the dose were adjusted at every visit as needed.

Background therapy:

NA

Evidence for comparator:

NA

| | |
|---|---|
| Actual start date of recruitment | 19 December 2017 |
| 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 | Armenia: 10 |
| Country: Number of subjects enrolled | Australia: 5 |
| Country: Number of subjects enrolled | Belarus: 5 |
| Country: Number of subjects enrolled | Canada: 1 |
| Country: Number of subjects enrolled | Georgia: 10 |
| Country: Number of subjects enrolled | New Zealand: 9 |
| Country: Number of subjects enrolled | Russian Federation: 50 |
| Country: Number of subjects enrolled | Turkey: 3 |
| Country: Number of subjects enrolled | Ukraine: 11 |
| Country: Number of subjects enrolled | United States: 174 |
| Country: Number of subjects enrolled | Poland: 8 |
| Country: Number of subjects enrolled | Romania: 3 |
| Country: Number of subjects enrolled | Bulgaria: 3 |
| Country: Number of subjects enrolled | Greece: 3 |
| Country: Number of subjects enrolled | Italy: 3 |

| | |
|---|---|
| Worldwide total number of subjects | 298 |
| EEA total number of subjects | 20 |

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) | 1 |
| Children (2-11 years) | 196 |
| Adolescents (12-17 years) | 101 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Overall, 298 subjects entered the extension trial from the parent trials: 103 subjects from the CT-301 Lonapegsomatropin group, 55 subjects from the CT-301 Genotropin group, and 140 subjects from the CT-302 Lonapegsomatropin group.

### Pre-assignment

Screening details:

Patients who completed a prior phase 3 lonapegsomatropin trial were screened. Patients with poorly controlled diabetes or diabetic complications, or with evidence of closed epiphyses or known hypersensitivity to the trial medication were excluded.
All inclusion/exclusion criteria were met during enrollment.

### 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:

Open-label study.

### Arms

| **Arm title** | Total |
|---|---|
| Arm description: - | |
| Arm type | Single arm |
| Investigational medicinal product name | lonapegsomatropin |
| Investigational medicinal product code | |
| Other name | TransCon hGH |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Lonapegsomatropin was provided in single-use glass vials and administered with syringe and needle, initially at a strength of 12.1 mg hGH/vial and subsequently at either 12.1 mg hGH/vial or 24.2 mg hGH/vial. The GH autoinjector was developed and approved and became available during the course of the extension trial for US participants. Lonapegsomatropin was supplied in dual-chamber cartridges (DCCs) for administration using a GH auto-injector (in the United States only). The DCC contained lyophilized drug product in one chamber and sterile water for injection diluent in the other chamber. The GH auto-injector, through a series of steps, automatically reconstituted the trial drug.

| **Number of subjects in period 1** | Total |
|---|---|
| Started | 298 |
| Completed | 259 |
| Not completed | 39 |
| Physician decision | 1 |
| Consent withdrawn by subject | 16 |
| Other | 10 |
| Lost to follow-up | 9 |

| | |
|---|---|
| Protocol deviation | 3 |

## Baseline characteristics

### Reporting groups

| Reporting group title | Treatment period |
|---|---|

Reporting group description: -

| Reporting group values | Treatment period | Total | |
|---|---|---|---|
| Number of subjects | 298 | 298 | |
| Age categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 1 | 1 | |
| Children (2-11 years) | 196 | 196 | |
| Adolescents (12-17 years) | 101 | 101 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 10.27 | | |
| standard deviation | ± 3.421 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 63 | 63 | |
| Male | 235 | 235 | |
| Tanner stage<br>Units: Subjects | | | |
| Tanner 1 | 214 | 214 | |
| Tanner 2 | 40 | 40 | |
| Tanner 3 | 25 | 25 | |
| Tanner 4 | 16 | 16 | |
| Tanner 5 | 3 | 3 | |
| Height SDS<br>Units: NA | | | |
| arithmetic mean | -1.564 | | |
| standard deviation | ± 0.878 | - | |
| IGF-1 SDS<br>Units: NA | | | |
| arithmetic mean | 0.515 | | |
| standard deviation | ± 1.579 | - | |

### Subject analysis sets

| Subject analysis set title | Full analysis set |
|---|---|
| Subject analysis set type | Full analysis |

Subject analysis set description:

Full analysis set included all subjects who signed inform consent for this extension trial and received at least one dose of trial drug.

| **Reporting group values** | Full analysis set | | |
|---|---|---|---|
| Number of subjects | 298 | | |
| Age categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 1 | | |
| Children (2-11 years) | 196 | | |
| Adolescents (12-17 years) | 101 | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 10.27 | | |
| standard deviation | ± 3.41 | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 63 | | |
| Male | 235 | | |
| Tanner stage<br>Units: Subjects | | | |
| Tanner 1 | 214 | | |
| Tanner 2 | 40 | | |
| Tanner 3 | 25 | | |
| Tanner 4 | 16 | | |
| Tanner 5 | 3 | | |
| Height SDS<br>Units: NA | | | |
| arithmetic mean | -1.564 | | |
| standard deviation | ± 0.878 | | |
| IGF-1 SDS<br>Units: NA | | | |
| arithmetic mean | 0.515 | | |
| standard deviation | ± 1.579 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Total |
| Reporting group description: - | |
| Subject analysis set title | Full analysis set |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Full analysis set included all subjects who signed inform consent for this extension trial and received at least one dose of trial drug.

### Primary: Number of subjects with treatment-emergent adverse events

| | |
|---|---|
| End point title | Number of subjects with treatment-emergent adverse events[1] |

End point description:

| | |
|---|---|
| End point type | Primary |

End point timeframe:

From ICF signature until end of study.

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: This is an open-label, long-term extension study, no statistical analyses were conducted.

| End point values | Full analysis set | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 298 | | | |
| Units: subjects with TEAE | 226 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Annualized Height Velocity - Week 13

| | |
|---|---|
| End point title | Annualized Height Velocity - Week 13 |

End point description:

For annualized height velocity, a rolling baseline was used to ensure a one-year span in the calculation.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

From baseline until Week 13.

| End point values | Full analysis set | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 295 | | | |
| Units: cm/year | | | | |
| arithmetic mean (standard deviation) | 8.904 (± 2.795) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Annualized Height Velocity - Week52

| End point title | Annualized Height Velocity - Week52 |
|---|---|

End point description:

For annualized height velocity, a rolling baseline was used to ensure a one-year span in the calculation.

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline until week 52.

| End point values | Full analysis set | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 284 | | | |
| Units: cm/year | | | | |
| arithmetic mean (standard deviation) | 8.560 (± 1.801) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Annualized Height Velocity - Week 104

| End point title | Annualized Height Velocity - Week 104 |
|---|---|

End point description:

For annualized height velocity, a rolling baseline was used to ensure a one-year span in the calculation.

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline until Week 104.

| End point values | Full analysis set | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 255 | | | |
| Units: cm/year | | | | |
| arithmetic mean (standard deviation) | 7.854 (± 1.953) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Annualized Height Velocity - Week 156

| End point title | Annualized Height Velocity - Week 156 |
|---|---|

End point description:

For annualized height velocity, a rolling baseline was used to ensure a one-year span in the calculation.

| End point type | Secondary |
|---|---|

End point timeframe:

From Week 104 until Week 156.

| End point values | Full analysis set | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 236 | | | |
| Units: cm/year | | | | |
| arithmetic mean (standard deviation) | 7.081 (± 1.838) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Annualized Height Velocity - Week 208

| End point title | Annualized Height Velocity - Week 208 |
|---|---|

End point description:

For annualized height velocity, a rolling baseline was used to ensure a one-year span in the calculation.

| End point type | Secondary |
|---|---|

End point timeframe:

From Week 156 until Week 208.

| End point values | Full analysis set | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 148 | | | |
| Units: cm/year | | | | |
| arithmetic mean (standard deviation) | 6.462 (± 1.868) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: IGF-1 SDS - Week 13

| End point title | IGF-1 SDS - Week 13 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline until Week 13

| End point values | Total | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 290 | | | |
| Units: SDS | | | | |
| arithmetic mean (standard deviation) | 1.210 (± 1.400) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: IGF-1 SDS - Week 52

| End point title | IGF-1 SDS - Week 52 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline until week 52.

| End point values | Total | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 282 | | | |
| Units: SDS | | | | |
| arithmetic mean (standard deviation) | 1.355 (± 1.231) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: IGF-1 SDS - Week 104

| End point title | IGF-1 SDS - Week 104 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline until week 104.

| End point values | Total | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 249 | | | |
| Units: SDS | | | | |
| arithmetic mean (standard deviation) | 1.613 (± 1.189) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: IGF-1 SDS - Week 156

| End point title | IGF-1 SDS - Week 156 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline until week 156.

| End point values | Total | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 231 | | | |
| Units: SDS | | | | |
| arithmetic mean (standard deviation) | 1.453 (± 1.125) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: IGF-1 SDS - Week 208

| End point title | IGF-1 SDS - Week 208 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline until week 208.

| End point values | Total | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 142 | | | |
| Units: SDS | | | | |
| arithmetic mean (standard deviation) | 1.597 (± 1.177) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Height SDS - Change from baseline - week 13

| End point title | Height SDS - Change from baseline - week 13 |
|---|---|

End point description:

Change from baseline in height SDS until Week 13.

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline until week 13.

| End point values | Full analysis set | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 295 | | | |
| Units: SDS | | | | |
| arithmetic mean (standard deviation) | 0.141 (± 0.125) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Height SDS - Change from baseline - week 52

| End point title | Height SDS - Change from baseline - week 52 |
|---|---|
| End point description: | |
| Change from baseline in height SDS until week 52. | |
| End point type | Secondary |
| End point timeframe: | |
| From baseline until week 52. | |

| End point values | Full analysis set | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 284 | | | |
| Units: SDS | | | | |
| arithmetic mean (standard deviation) | 0.491 (± 0.307) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Height SDS - Change from baseline - week 104

| End point title | Height SDS - Change from baseline - week 104 |
|---|---|
| End point description: | |
| Change from baseline in height SDS until week 104. | |
| End point type | Secondary |
| End point timeframe: | |
| From baseline until week 104. | |

| End point values | Full analysis set | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 255 | | | |
| Units: SDS | | | | |
| arithmetic mean (standard error) | 0.841 (± 0.487) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Height SDS - Change from baseline - week 156

| End point title | Height SDS - Change from baseline - week 156 |
|---|---|
| End point description: | |
| Change from baseline in height SDS until week 156. | |
| End point type | Secondary |
| End point timeframe: | |
| From baseline until week 156. | |

| End point values | Full analysis set | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 236 | | | |
| Units: SDS | | | | |
| arithmetic mean (standard deviation) | 1.089 (± 0.534) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Height SDS - Change from baseline - week 208

| End point title | Height SDS - Change from baseline - week 208 |
|---|---|
| End point description: | |
| Change from baseline in height SDS until week 208. | |
| End point type | Secondary |
| End point timeframe: | |
| From baseline until week 208. | |

| End point values | Full analysis set | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 148 | | | |
| Units: SDS | | | | |
| arithmetic mean (standard deviation) | 1.242 (± 0.652) | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From ICF signature up to 14 days after the final dose.

Adverse event reporting additional description:

AEs that were considered mild and not related to study drug were not be reported on the AE CRF. Reportable AEs either observed by the investigator or reported by the subject were recorded regardless of causality.
Treatment-emergent adverse events are considered (an AE was considered treatment-emergent if the event first occurred or worsened after)

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 25.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Full analysis set |

Reporting group description: -

| **Serious adverse events** | Full analysis set | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 21 / 298 (7.05%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Forearm fracture | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Humerus fracture | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Limb injury | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lip injury | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper limb fracture | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Congenital, familial and genetic disorders | | | |
| Diverticulitis Meckel's | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Brain stem infarction | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Epilepsy | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Generalised tonic-clonic seizure | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Headache | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---|---|---|
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Serum sickness-like reaction | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Cyclic vomiting syndrome | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Nephrotic syndrome | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---|---|---|
| Scoliosis | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 3 / 298 (1.01%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 298 (0.67%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abscess | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis salmonella | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tonsillitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 298 (0.34%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Full analysis set | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 225 / 298 (75.50%) | | |
| Investigations | | | |
| SARS-CoV-2 test positive | | | |
| subjects affected / exposed | 17 / 298 (5.70%) | | |
| occurrences (all) | 17 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 35 / 298 (11.74%) | | |
| occurrences (all) | 73 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 37 / 298 (12.42%) | | |
| occurrences (all) | 56 | | |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 19 / 298 (6.38%) | | |
| occurrences (all) | 24 | | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 24 / 298 (8.05%) | | |
| occurrences (all) | 33 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 28 / 298 (9.40%) | | |
| occurrences (all) | 52 | | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 65 / 298 (21.81%) | | |
| occurrences (all) | 164 | | |
| COVID-19 | | | |
| subjects affected / exposed | 40 / 298 (13.42%) | | |
| occurrences (all) | 41 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 40 / 298 (13.42%) | | |
| occurrences (all) | 68 | | |
| Influenza | | | |
| subjects affected / exposed | 30 / 298 (10.07%) | | |
| occurrences (all) | 36 | | |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 27 / 298 (9.06%) | | |
| occurrences (all) | 46 | | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 22 / 298 (7.38%) | | |
| occurrences (all) | 48 | | |
| Ear infection | | | |
| subjects affected / exposed | 18 / 298 (6.04%) | | |
| occurrences (all) | 30 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 17 / 298 (5.70%) | | |
| occurrences (all) | 22 | | |
| Bronchitis | | | |
| subjects affected / exposed | 15 / 298 (5.03%) | | |
| occurrences (all) | 23 | | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 15 / 298 (5.03%) | | |
| occurrences (all) | 16 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 29 January 2020 | Dual-chamber cartridge and GH auto-injection were introduced and rolled out to subjects (after introducing to the US on 04-Mar-2019 during a country-specific amendment), device usability questionnaire was added to assessments.<br>The definition of AEs was unified and clarified (routine titrations are not considered as AEs, asymptomatic out-of-range laboratory values may be AEs if they induce a new/worsening diagnosis or require therapy, out-of-range IGF-1, and IGFBP3 would not be considered as AEs, unless if they were associated with a diagnosis). |

Notes:

### 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.

Mostly boys were enrolled, the study population size of 298 subjects.

Notes:

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/35428884