



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
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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)	EMA-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
Consent withdrawn by subject	16
Physician decision	1
Other	10
Lost to follow-up	9

Protocol deviation	3
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Baseline characteristics

Reporting groups

Reporting group title	Treatment period
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Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	298	298	
Age categorical			
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			
Units: years			
arithmetic mean	10.27		
standard deviation	± 3.421	-	
Gender categorical			
Units: Subjects			
Female	63	63	
Male	235	235	
Tanner stage			
Units: Subjects			
Tanner 1	214	214	
Tanner 2	40	40	
Tanner 3	25	25	
Tanner 4	16	16	
Tanner 5	3	3	
Height SDS			
Units: NA			
arithmetic mean	-1.564		
standard deviation	± 0.878	-	
IGF-1 SDS			
Units: NA			
arithmetic mean	0.515		
standard deviation	± 1.579	-	

Subject analysis sets

Subject analysis set title	Full analysis set
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Subject analysis set type	Full analysis
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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 Units: Subjects			
Infants and toddlers (28 days-23 months)	1		
Children (2-11 years)	196		
Adolescents (12-17 years)	101		
Age continuous Units: years			
arithmetic mean	10.27		
standard deviation	± 3.41		
Gender categorical Units: Subjects			
Female	63		
Male	235		
Tanner stage Units: Subjects			
Tanner 1	214		
Tanner 2	40		
Tanner 3	25		
Tanner 4	16		
Tanner 5	3		
Height SDS Units: NA			
arithmetic mean	-1.564		
standard deviation	± 0.878		
IGF-1 SDS 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 informed 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 (\pm 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 (\pm 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 (\pm 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 (\pm 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 (\pm 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 (\pm 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 (\pm 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 (\pm 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 (\pm 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 (\pm 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 (\pm 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 (\pm 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 (\pm 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 (\pm 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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1
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Reporting groups

Reporting group title	Full analysis set
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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. 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>