Clinical trial results:
Open label, group comparison, dose escalation trial to investigate safety, tolerability, pharmacokinetics and pharmacodynamics of macimorelin acetate after single oral dosing of 0.25 mg/kg, 0.5 mg/kg, and 1 mg/kg in pediatric patients with suspected growth hormone deficiency (GHD)

Summary

EudraCT number	2018-001988-23
Trial protocol	HU PL
Global end of trial date	24 January 2020

Results information

Result version number	v1 (current)
This version publication date	09 August 2020
First version publication date	09 August 2020

Trial information

Trial identification

Sponsor protocol code	AEZS-130-P01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Study P01: Study P01

Notes:

Sponsors

Sponsor organisation name	Aeterna Zentaris GmbH
Sponsor organisation address	Weismuellerstr. 50, Frankfurt am Main, Germany, 60314
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001988-PIP01-16
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	17 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 January 2020
Global end of trial reached?	Yes
Global end of trial date	24 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary:
• To investigate the safety and tolerability of macimorelin acetate after ascending single oral doses of macimorelin in pediatric patients with suspected GHD.
Secondary:
• To investigate the PK of macimorelin acetate in pediatric patients with suspected GHD;
• To investigate the PD of macimorelin acetate as measured by GH release in pediatric patients with suspected GHD;
• To explore the PK/PD relationship following single oral dose administration of macimorelin acetate in pediatric patients with suspected GHD.

Protection of trial subjects:

All patients were informed that they had the right to withdraw from the trial at any time, for any reason, without prejudice, and without having to justify their reasons or decisions. Additionally, the investigator might have discontinued patient's participation at any time if he/she would have considered that to be in the patient's best interest or if the investigator determined that continuing the participation would have resulted in a significant safety risk for that patient.
Pediatic patients had to meet specific inclusion criterion to be eligible for admission to the trial, and they were ineligible to participate if meeting specific exclusion criteria. Once all the screening data became available, investigator performed the final evaluation of the patient's eligibility in the eCRF and forwarded it to the Medical Monitor (MM) for a final review. The MM confirmed eligibility in the eCRF.
The DRC comprised a panel of selected experts and a representative of the Sponsor.
The dose titration program was reconsidered after completion of each dose step and would proceed only if the previous dose step reviewed and confirmed by the DRC had shown acceptable safety and tolerability.
Sequential cohorts of trial participants received macimorelin at ascending single oral doses, The dose titration program was reconsidered after completion of each dose step and would proceed only if the previous dose step reviewed and confirmed by Data Review Committee (DRC) had shown acceptable safety and tolerability. This DRC comprised a panel of selected experts and a representative of the Sponsor.
The investigational medicinal product (IMP) macimorelin was administered by trial personnel experience in pediatrics.
A growth hormone stimulation test (GHST) Tolerability Questionniare was completed by patients or parents/legal guardians. It included specific questions regarding the acceptability of taste, any signs for an impact on sleep, appetite and gastrointestinal Symptoms.

Background therapy:

The selection of the two different sGHSTs followed the respective trial site's clinical standard practice and, therefore, the test agents used were considered as 'background' and not as 'investigational' medicinal products.
The following pharmacological agents were accepted for sGHSTs performed as part of the standard procedures for diagnosing GHD in pediatric patients:
Insulin tolerance test (ITT), Arginine, Arginine/Growth hormone releasing hormone (GHRH), Clonidine, Glucagon, L-dopa.

Evidence for comparator:

This was a dose-escalation, PK/PD study. No comparators were used.

Actual start date of recruitment	01 November 2018
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	Poland: 2
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Ukraine: 10
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Belarus: 1
Country: Number of subjects enrolled	Serbia: 2
Worldwide total number of subjects	24
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)	13
Adolescents (12-17 years)	11
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial started on 07-Feb-2019 with the first informed consent signed. The first sGHST was administered in Cohort 1 (C1) on 13-Feb-2019. In C1, the first macimorelin test was conducted on 28-Feb-2019, in Cohort 2 (C2) on 08-Jul-2019, and in Cohort 3 (C3) on 05-Dec-2019. The trial was completed with Last-Patient-Last-Visit on 24-Jan-2020.

Pre-assignment

Screening details:

Altogether 27 patients consented to trial participation in 11 trial centers in 6 countries. 24 patients had an evaluable first standard Growth Hormone Stimulation test and, thus, were considered as enrolled in the Trial.

Period 1

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

Blinding implementation details:

The trial was conducted open-label as trial medication and procedures cannot be masked. Macimorelin was administered as oral solution. The sGHSTs were considered as 'background' (i.e., standard medication) and not as IMPs. Depending on the sGHSTs selected by the trial site, the test agents were administered i.v., i.m., s.c., or peroral.
The Investigators were blinded towards GH values (test results) until both sGHSTs were performed and adjudicated evaluable by the DRC.

Arms

Are arms mutually exclusive?	Yes
Arm title	Macimorelin GHST: C1

Arm description:

This is the first of three cohorts assessing ascending doses of macimorelin (one dose per pediatric patient). C1: macimorelin 0.25 mg/kg.
Each cohort is comprising 8 pediatric patients.

Arm type	Experimental
Investigational medicinal product name	C1: macimorelin 0.25 mg/kg
Investigational medicinal product code	AEZS-130
Other name	macimorelin Growth Hormone Stimulation Test (GHST); macimorelin GHST
Pharmaceutical forms	Granules in sachet
Routes of administration	Oral use

Dosage and administration details:

Macimorelin was supplied in single-use aluminum pouches (synonymous: sachets) each containing 63.6 mg macimorelin acetate, which provide 0.5 mg/mL of macimorelin when dissolved in 120 mL of water. Macimorelin had to be prepared and used according to specific directions for the three dosing groups. Applicable for C1: based on the macimorelin dose of 0.25 mg/kg, the required volume of the suspension was to be determined which corresponded to the patient body weight, i.e. required volume of suspension was 0.5 mL/kg (for example, a 30 kg patient requiring macimorelin dose of 0.25 mg/kg required 15 mL of the prepared suspension).

Arm title	Macimorelin GHST: C2

Arm description:

This is the second of three cohorts assessing ascending doses of macimorelin (one dose per pediatric patient). C2: macimorelin 0.50 mg/kg.
Each cohort is comprising 8 pediatric patients.

Arm type	Experimental

Investigational medicinal product name	C1: macimorelin 0.5 mg/kg
Investigational medicinal product code	AEZS-130
Other name	macimorelin Growth Hormone Stimulation Test (GHST); macimorelin GHST
Pharmaceutical forms	Granules in sachet
Routes of administration	Oral use

Dosage and administration details:

Macimorelin was supplied in single-use aluminum pouches (synonymous: sachets) each containing 63.6 mg macimorelin acetate, which provide 0.5 mg/mL of macimorelin when dissolved in 120 mL of water. Macimorelin had to be prepared and used according to specific directions for the three dosing groups. Applicable for C2: based on the macimorelin dose of 0.5 mg/kg, the required volume of the suspension was to be determined which corresponded to the patient body weight, i.e. required volume of suspension was 1.0 mL/kg (for example, a 30 kg patient requiring macimorelin dose of 0.5 mg/kg required 30 mL of the prepared suspension).

Arm title	Macimorelin GHST: C3

Arm description:

This is the third of three cohorts assessing ascending doses of macimorelin (one dose per pediatric patient). C3: macimorelin 1.0 mg/kg.
Each cohort is comprising 8 pediatric patients.

Arm type	Experimental
Investigational medicinal product name	C1: macimorelin 1.0 mg/kg
Investigational medicinal product code	AEZS-130
Other name	macimorelin Growth Hormone Stimulation Test (GHST); macimorelin GHST
Pharmaceutical forms	Granules in sachet
Routes of administration	Oral use

Dosage and administration details:

Macimorelin was supplied in single-use aluminum pouches (synonymous: sachets) each containing 63.6 mg macimorelin acetate, which provide 0.5 mg/mL of macimorelin when dissolved in 120 mL of water. Macimorelin had to be prepared and used according to specific directions for the three dosing groups. Applicable for C3: based on the macimorelin dose of 1.0 mg/kg, the required volume of the suspension was to be determined which corresponded to the patient body weight, i.e. required volume of suspension was 2.0 mL/kg (for example, a 30 kg patient requiring macimorelin dose of 1.0 mg/kg required 60 mL of the prepared suspension).

Number of subjects in period 1	Macimorelin GHST: C1	Macimorelin GHST: C2	Macimorelin GHST: C3
Started	8	8	8
Completed	8	8	8

Baseline characteristics

Reporting groups	
Reporting group title	Macimorelin GHST: C1
Reporting group description:	
This is the first of three cohorts assessing ascending doses of macimorelin (one dose per pediatric patient). C1: macimorelin 0.25 mg/kg. Each cohort is comprising 8 pediatric patients.	
Reporting group title	Macimorelin GHST: C2
Reporting group description:	
This is the second of three cohorts assessing ascending doses of macimorelin (one dose per pediatric patient). C2: macimorelin 0.50 mg/kg. Each cohort is comprising 8 pediatric patients.	
Reporting group title	Macimorelin GHST: C3
Reporting group description:	
This is the third of three cohorts assessing ascending doses of macimorelin (one dose per pediatric patient). C3: macimorelin 1.0 mg/kg. Each cohort is comprising 8 pediatric patients.	

Reporting group values	Macimorelin GHST: C1	Macimorelin GHST: C2	Macimorelin GHST: C3
Number of subjects	8	8	8
Age categorical			
Information on patient's current age was collected at screening.			
Units: Subjects			
Children (2-11 years)	5	5	3
Adolescents (12-17 years)	3	3	5
Age continuous			
Information on patient's current age was collected at screening.			
Units: years			
median	10.5	8	12.5
standard deviation	± 3.5	± 4.2	± 3.9
Gender categorical			
Information on gender was collected at screening.			
Units: Subjects			
Female	3	3	1
Male	5	5	7
Tanner Status			
Information was collected at screening. At least 3 patients per dose group were required to be pre-pubertal (Tanner Stage I) and pubertal (Tanner Stage II-IV), respectively. In this study, Tanner stage of the patients was either Tanner Stage I or Tanner Stage II. No Tanner Stage III or IV were observed.			
Units: Subjects			
Tanner Stage I	4	5	4
Tanner Stage II	4	3	4
Race			
Information was collected at Screening.			
Units: Subjects			
Asian	0	0	0
Black of African-American	0	0	0
White	8	8	8
Specification of the two sGHSTs			
The selection of the two different sGHSTs at V1 and V3 followed the trial site’s clinical standard practice			

and, therefore, the test agents used were considered as 'background' and not as 'investigational' medicinal products. The figures bleow present a summary of the two sGHST agents administered to a pediatric patient.			
Units: Subjects			
Arginine Test and Insulin Tolerance Test	6	0	0
Clonidine Test and Insulin Tolerance Test	2	7	7
Glucagon Test and Arginine Test	0	1	1
Height			
Actual height was measured at Screening.			
Units: cm			
median	114.8	117.65	137.60
standard deviation	± 32.79	± 20.95	± 19.67
Weight			
Body weight was recorded at Screening, at Visit 1 and Visit 3 (before the sGHST), and at Visit 2(before the macimorelin test). It was to be recorded in kg (rounded to closest integer). The values presented here were collected at Screening.			
Units: kg			
median	19.5	27.5	30.5
standard deviation	± 10.1	± 10.9	± 10.0
Height Standard Deviation Score (SDS)			
Auxology Parameters were collected at Screening.			
Units: SDS			
median	-2.50	-2.20	-2.45
standard deviation	± 0.50	± 1.47	± 0.58
Annualized Height Velocity SDS			
Auxology Parameters were collected at Screening.			
Units: SDS			
median	-1.90	-1.50	-0.65
standard deviation	± 1.09	± 1.10	± 1.12

Reporting group values	Total		
Number of subjects	24		
Age categorical			
Information on patient's current age was collected at screening.			
Units: Subjects			
Children (2-11 years)	13		
Adolescents (12-17 years)	11		
Age continuous			
Information on patient's current age was collected at screening.			
Units: years			
median			
standard deviation	-		
Gender categorical			
Information on gender was collected at screening.			
Units: Subjects			
Female	7		
Male	17		
Tanner Status			
Information was collected at screening. At least 3 patients per dose group were required to be pre-pubertal (Tanner Stage I) and pubertal (Tanner Stage II-IV), respectively. In this study, Tanner stage of the patients was either Tanner Stage I or Tanner Stage II. No Tanner Stage III or IV were observed.			
Units: Subjects			

Tanner Stage I	13		
Tanner Stage II	11		
Race			
Information was collected at Screening.			
Units: Subjects			
Asian	0		
Black of African-American	0		
White	24		
Specification of the two sGHSTs			
The selection of the two different sGHSTs at V1 and V3 followed the trial site's clinical standard practice and, therefore, the test agents used were considered as 'background' and not as 'investigational' medicinal products. The figures bleow present a summary of the two sGHST agents administered to a pediatric patient.			
Units: Subjects			
Arginine Test and Insulin Tolerance Test	6		
Clonidine Test and Insulin Tolerance Test	16		
Glucagon Test and Arginine Test	2		
Height			
Actual height was measured at Screening.			
Units: cm			
median			
standard deviation	-		
Weight			
Body weight was recorded at Screening, at Visit 1 and Visit 3 (before the sGHST), and at Visit 2(before the macimorelin test). It was to be recorded in kg (rounded to closest integer). The values presented here were collected at Screening.			
Units: kg			
median			
standard deviation	-		
Height Standard Deviation Score (SDS)			
Auxology Parameters were collected at Screening.			
Units: SDS			
median			
standard deviation	-		
Annualized Height Velocity SDS			
Auxology Parameters were collected at Screening.			
Units: SDS			
median			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Macimorelin GHST: C1
Reporting group description:	
This is the first of three cohorts assessing ascending doses of macimorelin (one dose per pediatric patient). C1: macimorelin 0.25 mg/kg. Each cohort is comprising 8 pediatric patients.	
Reporting group title	Macimorelin GHST: C2
Reporting group description:	
This is the second of three cohorts assessing ascending doses of macimorelin (one dose per pediatric patient). C2: macimorelin 0.50 mg/kg. Each cohort is comprising 8 pediatric patients.	
Reporting group title	Macimorelin GHST: C3
Reporting group description:	
This is the third of three cohorts assessing ascending doses of macimorelin (one dose per pediatric patient). C3: macimorelin 1.0 mg/kg. Each cohort is comprising 8 pediatric patients.	

Primary: Macimorelin PK

End point title	Macimorelin PK[1]
End point description:	
Plasma concentrations of macimorelin were analyzed in a central laboratory.	
End point type	Primary
End point timeframe:	
Blood samples were collected on V2 at the following time-points: pre-dose (sampling time window: +/- 15 minutes), then 15, 30, 45, 60, 90, 120 minutes (+/- 5 min window) and 360 minutes (+/- 10 minutes window) after administration of macimorelin.	

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: The trial had an explorative, descriptive aim and did not intend to prove or disprove any statistical hypothesis. Furthermore, the statistical analyses sections in this electronic reporting template do not fit with the way the explorative data analyses were conducted in this Trial (e.g., ROC, sensitivity, specificity analyses). Related data are presented in the 'Endpoints'. Therefore, the statistical analyses sections are empty.

End point values	Macimorelin GHST: C1	Macimorelin GHST: C2	Macimorelin GHST: C3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	8	8	
Units: Macimorelin concentration				
arithmetic mean (standard deviation)				
AUC 0-6 (h*ng/mL)	6.685 (± 3.093)	18.015 (± 9.800)	30.920 (± 11.510)	
Cmax (ng/mL)	3.460 (± 1.783)	8.126 (± 4.176)	12.868 (± 3.011)	
Tmax (min)	45.5 (± 32.8)	40.6 (± 22.3)	31.9 (± 5.3)	
T1/2 (min)	73.183 (± 29.437)	96.307 (± 41.031)	102.851 (± 19.938)	

Statistical analyses

No statistical analyses for this end point

Primary: Macimorelin PD

End point title	Macimorelin PD[2]

End point description:

Serum concentrations of growth hormone (GH) were analyzed in a central laboratory.

End point type	Primary

End point timeframe:

Blood samples were collected on V2 at the following time-points: pre-dose (sampling time window: +/- 15 minutes), then 15, 30, 45, 60, 90, 120 minutes (+/- 5 min window) and 360 minutes (+/- 10 minutes window) after administration of macimorelin.

Notes:

[2] - 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: The trial had an explorative, descriptive aim and did not intend to prove or disprove any statistical hypothesis. Furthermore, the statistical analyses sections in this electronic reporting template do not fit with the way the explorative data analyses were conducted in this Trial (e.g., ROC, sensitivity, specificity analyses). Related data are presented in the 'Endpoints'. Therefore, the statistical analyses sections are empty.

End point values	Macimorelin GHST: C1	Macimorelin GHST: C2	Macimorelin GHST: C3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	8	8	
Units: growth hormone concentration				
arithmetic mean (standard deviation)				
Cmax (ng/mL)	9.791 (± 6.226)	14.590 (± 8.046)	29.533 (± 18.829)	
Tmax (min)	52.5 (± 11.3)	37.5 (± 13.9)	37.5 (± 8.0)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Macimorelin GHST versus PI Assessment and versus sGHST

End point title	Macimorelin GHST versus PI Assessment and versus sGHST

End point description:

The diagnostic outcome of the sGHST was considered as ‘confirmed’ if both sGHSTs were available and both resulted in a peak GH ≤ 7 ng/mL or ‘not confirmed’ of at least one of the peaks was above 7 ng/mL. The investigator’s assessment was based on local diagnostic standard practice. The macimorelin GHST was tested against a cut-off point calculated from the individual peak GH values.

End point type	Other pre-specified

End point timeframe:

Macimorelin GHST (MAC) was performed on V2, and sGHSTs on V1 and V3. Blood sampling for MAC at pre-dose, 15, 30, 45, 60, 90, 120 min. (+/- 5 min) , 360 min. (+/- 10 min.), for sGHSTs at time points according to local Standards.

End point values	Macimorelin GHST: C1	Macimorelin GHST: C2	Macimorelin GHST: C3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8[3]	8[4]	8[5]	
Units: pediatric patients				
PI's Assessment GHD - MAC confirmed	3	4	3	
PI's Assessment GHD - MAC not confirmed	0	1	0	
PI's Assessment Non GHD - MAC confirmed	3	0	1	
PI's Assessment Non GHD - MAC not confirmed	2	3	4	
sGHST confirmed - MAC confirmed	1	3	3	
sGHST confirmed - MAC not confirmed	0	1	0	
sGHST not confirmed - MAC confirmed	5	1	1	
sGHST not confirmed - MAC not confirmed	2	3	4	

Notes:

[3] - Exploratory GH cut-off point for the macimorelin GHST in C1: 10.030 ng/mL

[4] - Exploratory GH cut-off point for the macimorelin GHST in C2: 10.430 ng/mL

[5] - Exploratory GH cut-off point for the macimorelin GHST in C3: 17.130 ng/mL

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Exploration of a suitable GH cut-off point for the macimorelin GHST

End point title	Exploration of a suitable GH cut-off point for the macimorelin GHST

End point description:

ROC curves were created to plot the sensitivity and specificity of all possible peak GH values after macimorelin GHST at the categorization of subjects with GHD vs. non GHD based on investigator's assessment. Cut-off point with the maximum Youden index value was selected by cohort. In case of equivalence, cut-off point with higher sensitivity was chosen.
Weighted Youden index was calculated with having more weight on sensitivity. The weight for the Youden index was 0.6 and 0.7. The following formula was used for the calculation: Weighted Youden index= 2w SEN + 2 (1-w) SPEC - 1.
Specificity, sensitivity, negative predictive value (NPV), positive predictive value (PPV) and weighted Youden index are presented by cohort. As a sensitivity analysis, three different GH cut-off points were selected based on the categorization of subjects with standard GHST considering 'confirmed' vs. 'not confirmed' cases.

End point type	Other pre-specified

End point timeframe:

Macimorelin GHST (MAC) was performed on V2, and sGHSTs on V1 and V3. Blood sampling for MAC at pre-dose, 15, 30, 45, 60, 90, 120 min. (+/- 5 min) , 360 min. (+/- 10 min.), for sGHSTs at time points according to local Standards.

End point values	Macimorelin GHST: C1	Macimorelin GHST: C2	Macimorelin GHST: C3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	8	8	
Units: GH peak values				
number (not applicable)				
peak GH cut-off point (ng/mL)	10.030	10.430	17.130	
Specificity	0.40	1.00	0.80	
Sensitivity	1.00	0.80	1.00	
Youden-Index	0.40	0.80	0.80	
Weighted Youden-Index (w=0.6)	0.52	0.76	0.84	
Weighted Youden-Index (w=0.7)	0.64	0.72	0.88	
Negative Predictive Value	1.00	0.75	1.00	
Positive Predictive Value	0.50	1.00	0.75	
ROC AUC	0.60	0.80	0.93	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were recorded from after the moment of signing ICF and up to the end of the trial (V4), i.e. from Day -28 to D-1 (Screening) up to D19+ (V4).

Adverse event reporting additional description:

No AE was reported in relationship to macimorelin. No serious AE (SAE) was reported in this study. Majority of AEs was related to the Insulin tolerance test (ITT). AEs were mostly of mild to moderate intensity. Known side effects were reported for sGHST. ITT related AES comprised symptoms of hypoglycemia, which is a clinical endpoint of this sGHST.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	C1 macimorelin GHST

Reporting group description:

This group includes all pediatric patients observed in C1.

Reporting group title	C2 macimorelin GHST

Reporting group description:

This group includes all pediatric patients observed in C2.

Reporting group title	C3 macimorelin GHST

Reporting group description:

This group includes all pediatric patients observed in C3.

Serious adverse events	C1 macimorelin GHST	C2 macimorelin GHST	C3 macimorelin GHST
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	C1 macimorelin GHST	C2 macimorelin GHST	C3 macimorelin GHST
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	8 / 8 (100.00%)	7 / 8 (87.50%)
Investigations			
Blood pressure diastolic decreased	Additional description: Blood pressure diastolic decreased was reported in relationship to the clonidine GHST.		
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2

Blood pressure systolic decreased	Additional description: Blood pressure systolic decreased was reported in relationship to the clonidine GHST.		
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	3 / 8 (37.50%)
occurrences (all)	0	0	3
Vascular disorders			
Pallor	Additional description: Pallor was reported in relationship to the ITT.		
subjects affected / exposed	0 / 8 (0.00%)	2 / 8 (25.00%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Cardiac disorders			
Palpitations	Additional description: Palpitations were reported in relationship to the hypoglycemia, which is an expected endpoint of the ITT.		
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Tachycardia	Additional description: Tachycardia was reported in relationship to the hypoglycemia, which is an expected endpoint of the ITT.		
subjects affected / exposed	1 / 8 (12.50%)	4 / 8 (50.00%)	1 / 8 (12.50%)
occurrences (all)	1	4	1
Nervous system disorders			
Somnolence	Additional description: Somnolence was reported in relationship to the ITT as well as the clonidine GHST, and it is a known side effect of these sGHSTs.		
subjects affected / exposed	3 / 8 (37.50%)	2 / 8 (25.00%)	3 / 8 (37.50%)
occurrences (all)	4	2	3
Tremor	Additional description: Tremor was reported in relationship to the hypoglycemia, which is an expected endpoint of the ITT.		
subjects affected / exposed	2 / 8 (25.00%)	1 / 8 (12.50%)	3 / 8 (37.50%)
occurrences (all)	2	1	3
Dizziness	Additional description: Dizziness was reported in relationship to the hypoglycemia, which is an expected endpoint of the ITT.		
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	4 / 8 (50.00%)
occurrences (all)	0	0	4
Gastrointestinal disorders			
Hunger	Additional description: Hunger was reported in relationship to the ITT.		
subjects affected / exposed	6 / 8 (75.00%)	3 / 8 (37.50%)	1 / 8 (12.50%)
occurrences (all)	6	3	2
Skin and subcutaneous tissue disorders			
Hyperhidrosis	Additional description: Hyperhidrosis was reported in relationship to the hypoglycemia, which is an expected endpoint of the ITT.		
subjects affected / exposed	4 / 8 (50.00%)	5 / 8 (62.50%)	3 / 8 (37.50%)
occurrences (all)	4	5	3
Infections and infestations			
Bronchitis	Additional description: AE reported as not being related to an sGHST and/or the macimorelin GHST, respectively.		

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Oral herpes	Additional description: AE reported as not being related to an sGHST and/or the macimorelin GHST, respectively.		
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection	Additional description: AE reported as not being related to an sGHST and/or the macimorelin GHST, respectively.		
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection	Additional description: AE reported as not being related to an sGHST and/or the macimorelin GHST, respectively.		
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported