Clinical trial results:
Targeting the beta-2 adrenergic pathway to improve skeletal muscle glucose uptake in healthy humans

Summary

EudraCT number	2018-004245-16
Trial protocol	NL
Global end of trial date	23 April 2021

Results information

Result version number	v1 (current)
This version publication date	18 August 2022
First version publication date	18 August 2022

Trial information

Trial identification

Sponsor protocol code	NL67646.068.18

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Maastricht University
Sponsor organisation address	Universiteitssingel 50, Maastricht , Netherlands,
Public contact	Clinicaltrials.gov, Maastricht University, 0031 0433884254, Sten.vanbeek@maastrichtuniversity.nl
Scientific contact	Clinicaltrials.gov, Maastricht University, 0031 0433884254, Sten.vanbeek@maastrichtuniversity.nl

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	20 July 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 April 2021
Global end of trial reached?	Yes
Global end of trial date	23 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine if prolonged treatment with the selective beta-2-adrenergic agonist clenbuterol improves skeletal muscle glucose disposal via the mTORC2 pathway in lean, healthy male individuals with normal physical activity.

Protection of trial subjects:

Performed measurements will be without risks, but hematomas or bruises could develop upon blood sampling or muscle biopsies taken. This risk will be minimized due to state-of-the-art techniques and sterility measures taken. Clenbuterol or placebo supplementation will be given for 14 days, in which subjects ingest 1 capsule (20 microg) twice daily (40 microg/day). Clenbuterol could induce adverse effects, e.g. headache, increased heart rate/blood pressure, tremors, dizziness. To minimize the risks of adverse events, we deliberately choose to perform the study in a young, healthy population, using a standard dose clenbuterol (40 microg/day) as well as a short treatment duration. To limit the number of subjects that need to be included we decided for a cross-over design in which every participant serves as his own control.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 April 2019
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	Netherlands: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	12
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were screened for age and BMI

Period 1

Period 1 title	Placebo
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Arm title	Placebo

Arm description:

In a randomised, placebo-controlled, double-blinded, cross-over study, subjects received either clenbuterol hydrochloride or a placebo for 2 weeks. Afterwards, a 4-week wash-out was performed, after which subjects would receive another 2 weeks with the other compound that was not received in the first period

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Placebo for comparison

Number of subjects in period 1	Placebo
Started	12
Completed	11
Not completed	1
COVID-19 pandemic	1

Period 2

Period 2 title	Clenbuterol hydrochloride
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Arm title	Clenbuterol hydrochloride

Arm description:

In a randomised, placebo-controlled, double-blinded, cross-over study, subjects received either clenbuterol hydrochloride or a placebo for 2 weeks. Afterwards, a 4-week wash-out was performed, after which subjects would receive another 2 weeks with the other compound that was not received in the first period

Arm type	Experimental
Investigational medicinal product name	Clenbuterol hydrochloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Subjects received 2x 20 microg of clenbuterol daily (= 40 microg/day)

Number of subjects in period 2	Clenbuterol hydrochloride
Started	11
Completed	11

Baseline characteristics

Reporting groups

Reporting group title	Placebo

Reporting group description: -

Reporting group values	Placebo	Total	
Number of subjects	12	12	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
geometric mean	24.9		
standard deviation	± 3.7	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	12	12	
BMI Units: kg/m2			
geometric mean			
standard deviation	±	-	
Systolic blood pressure Units: mmHg			
geometric mean			
standard deviation	±	-	
Diastolic blood pressure Units: mmHg			
geometric mean			
standard deviation	±	-	
Heart rate Units: Beats/min			
geometric mean			
standard deviation	±	-	
ALAT Units: U/L			
geometric mean			
standard deviation	±	-	

ASAT Units: U/L geometric mean standard deviation	±	-	
gamma-GT Units: U/L geometric mean standard deviation	±	-	
Creatinine Units: micromole(s)/litre geometric mean standard deviation	±	-	
Haemoglobin Units: mmol/L geometric mean standard deviation	±	-	
Potassium Units: mmol/L geometric mean standard deviation	±	-	
TSH Units: mU/L geometric mean standard deviation	±	-	

Subject analysis sets

Subject analysis set title	Baseline characteristics
Subject analysis set type	Per protocol

Subject analysis set description:

Baseline characteristics

Reporting group values	Baseline characteristics		
Number of subjects	11		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years geometric mean standard deviation	24.9 ± 3.7		

Gender categorical Units: Subjects			
Female	0		
Male	11		
BMI Units: kg/m2			
geometric mean	23.1		
standard deviation	± 1.9		
Systolic blood pressure Units: mmHg			
geometric mean	120		
standard deviation	± 9.9		
Diastolic blood pressure Units: mmHg			
geometric mean	72		
standard deviation	± 6.7		
Heart rate Units: Beats/min			
geometric mean	58		
standard deviation	± 6.4		
ALAT Units: U/L			
geometric mean	25		
standard deviation	± 11		
ASAT Units: U/L			
geometric mean	23		
standard deviation	± 7		
gamma-GT Units: U/L			
geometric mean	19		
standard deviation	± 6		
Creatinine Units: micromole(s)/litre			
geometric mean	82		
standard deviation	± 7		
Haemoglobin Units: mmol/L			
geometric mean	9.6		
standard deviation	± 0.5		
Potassium Units: mmol/L			
geometric mean	4.25		
standard deviation	± 0.22		
TSH Units: mU/L			
geometric mean	2.2		
standard deviation	± 1.0		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
In a randomised, placebo-controlled, double-blinded, cross-over study, subjects received either clenbuterol hydrochloride or a placebo for 2 weeks. Afterwards, a 4-week wash-out was performed, after which subjects would receive another 2 weeks with the other compound that was not received in the first period	
Reporting group title	Clenbuterol hydrochloride
Reporting group description:	
In a randomised, placebo-controlled, double-blinded, cross-over study, subjects received either clenbuterol hydrochloride or a placebo for 2 weeks. Afterwards, a 4-week wash-out was performed, after which subjects would receive another 2 weeks with the other compound that was not received in the first period	
Subject analysis set title	Baseline characteristics
Subject analysis set type	Per protocol
Subject analysis set description:	
Baseline characteristics	

Primary: insulin-stimulated glucose disposal

End point title	insulin-stimulated glucose disposal
End point description:	
End point type	Primary
End point timeframe:	
2 weeks	

End point values	Clenbuterol hydrochloride	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: microM/kg/min				
geometric mean (standard error)	41.2 (± 2.7)	46.6 (± 3.5)		

Statistical analyses

Statistical analysis title	Analysis primary end point
Statistical analysis description:	
Data was compared with a Paired T-test due to cross-over design. Thus, all subjects were their own control.	
Comparison groups	Placebo v Clenbuterol hydrochloride

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.02
Method	t-test, 2-sided

Secondary: GLUT4 translocation

End point title	GLUT4 translocation

End point description:

End point type	Secondary

End point timeframe:

2-weeks

End point values	Clenbuterol hydrochloride	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Arbitrary units				
geometric mean (standard error)	56.1 (± 4.0)	55.4 (± 3.6)		

Statistical analyses

Statistical analysis title	statistical analyses secondary outcome

Statistical analysis description:

Data was compared with a Paired T-test due to cross-over design. Thus, all subjects were their own control.

Comparison groups	Clenbuterol hydrochloride v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.865 [1]
Method	t-test, 2-sided

Notes:

[1] - paired T-test

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 13-08-2019 till 23-04-2022	
Assessment type	Systematic
Dictionary used	
Dictionary name	NA
Dictionary version	0
Reporting groups	
Reporting group title	Clenbuterol hydrochloride

Reporting group description: -

Serious adverse events	Clenbuterol hydrochloride		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Clenbuterol hydrochloride		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 11 (45.45%)		
Nervous system disorders			
Tremor in hands			
subjects affected / exposed	5 / 11 (45.45%)		
occurrences (all)	5		
Feeling anxious / restless			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			

Muscle ache, tense muscles or cramps subjects affected / exposed occurrences (all)	4 / 11 (36.36%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 August 2019	Added flow-mediated dilation measurement to protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
16 March 2020	Due to the COVID-19 pandemic in the Netherlands, the study had been temporarily halted	01 July 2020

Notes:

Limitations and caveats

None reported