Clinical trial results:
A clinical study to assess the feasibility of measuring inhaled medication concentrations in exhaled breath condensate obtained from healthy volunteers and asthma patients and to assess the relationship with clinical endpoints

Summary

EudraCT number	2017-003177-34
Trial protocol	NL
Global end of trial date	20 August 2019

Results information

Result version number	v1 (current)
This version publication date	17 February 2022
First version publication date	17 February 2022

Trial information

Trial identification

Sponsor protocol code	CHDR1722

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Centre for Human Drug Research
Sponsor organisation address	Zernikedreef 8, Leiden, Netherlands, 2333CL
Public contact	Principal Investigator, Centre for Human Drug Research, +31 715246400, clintrials@chdr.nl
Scientific contact	Principal Investigator, Centre for Human Drug Research, +31 715246400, clintrials@chdr.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 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 August 2019
Global end of trial reached?	Yes
Global end of trial date	20 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objectives:
- To identify whether EBC can be used as a non-invasive method to measure the PK of salbutamol and tobramycin.
- To determine whether the relationship in mild-moderate asthmatics between pulmonary lung function parameters and salbutamol concentrations can be better described by concentrations in the EBC compared to plasma.

Protection of trial subjects:

Screening of 12 healthy male volunteers. Measurements: ECG, vitals, pulmonary function tests and bloodsamples for hematological and chemical analysis.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 December 2017
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:

Recruitment overall studyperiod

Pre-assignment

Screening details:

12 healthy male subjects, eligible according to in- and exclusion criteria after screening.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Salbutamol intravenous

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

A total dose of 250 microgram salbutamol (5 ml of 50mcg/ml) will be injected slowly i.v.in 1-10 minutes.

Arm title	Salbutamol inhaled

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

A total dose of 400 microgram will be administered using the Volumatic®device.

Arm title	Tobramycin intravenous

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Tobramycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

A total dose of 1mg/kg tobramycin will be administered i.v.. For this purpose the required dose of tobramycin 40 mg/ml will be solved in 50-100ml 0.9% Natriumchloride infusion fluid. The infusion will be administered in 30 minutes.
For subjects with a BMI >25the dose will be adjusted for body composition following the following

formula:
Dosing weight = Ideal body weight + 0.40 * (Actual body weight –Ideal body weight).
Ideal body weight = length (in meters) * length (in meters) * 25.

Arm title	Tobramycin inhaled
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Tobramycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

A total dose of 170 mg tobramycin will be administered by inhalation using the Medix AC2000®nebulizerof Clement Clarke International.

Number of subjects in period 1	Salbutamol intravenous	Salbutamol inhaled	Tobramycin intravenous
Started	12	12	12
Completed	12	12	12

Number of subjects in period 1	Tobramycin inhaled
Started	12
Completed	12

Baseline characteristics

Reporting groups	
Reporting group title	Overall studyperiod

Reporting group description: -

Reporting group values	Overall studyperiod	Total	
Number of subjects	12	12	
Age categorical Units: Subjects			
Adults (18-64 years)	12	12	
Gender categorical Units: Subjects			
Male	12	12	

End points

End points reporting groups

Reporting group title	Salbutamol intravenous
Reporting group description: -	
Reporting group title	Salbutamol inhaled
Reporting group description: -	
Reporting group title	Tobramycin intravenous
Reporting group description: -	
Reporting group title	Tobramycin inhaled
Reporting group description: -	

Primary: Treatment-emergent serious adverse events (SAEs)

End point title	Treatment-emergent serious adverse events (SAEs)[1]

End point description:

End point type	Primary

End point timeframe:

Overall studyperiod

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: As this was an exploratory study, no formal power analysis was performed. Pharmacokinetic endpoints were summarized descriptively.
Please refer to uploaded article.

End point values	Salbutamol intravenous	Salbutamol inhaled	Tobramycin intravenous	Tobramycin inhaled
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	12
Units: Number	0	0	0	0

Attachments (see zip file)	Report/Pharmacokinetics of intravenous and inhaled salbutamol

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20

Reporting groups	
Reporting group title	Studygroup

Reporting group description: -

Serious adverse events	Studygroup		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Studygroup		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)		
Cardiac disorders			
Palpitations			
subjects affected / exposed	10 / 12 (83.33%)		
occurrences (all)	10		
Dizziness			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
General disorders and administration site conditions			

Influenza like illness subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Feeling abnormal subjects affected / exposed occurrences (all) Feeling hot subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1		
Gastrointestinal disorders Dry mouth subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 March 2018	The change in this amendment covers the addition of two PK and EBC samples to the protoco
08 May 2018	additional spirometry measurements with a new spirometrydevice, which we want to validate during stage 2 of the study.
28 May 2018	-The upper limit for age is increased to 65 years; - The upper limit for BMI is increased to 35 kg/m2; - The minimum period subjects have to be off corticosteroid inhalation therapy has been reduced to threeweeks; and, - For the lung function a post-bronchodilator for FEVI > 70% of predicted will be used instead of pre-bronchodilator FEVr > 70% of predicted. As all asthma subjects will receive salbutamol, either inhaled orintravenously at the start of each the study days, a post bronchodilator lung function is more relevant. lnaddition, exhaled breath condensate sampling involves tidal breathing and is not associated withbronchoconstriction (Baraldi, 2003) .

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported