Clinical trial results:
Evaluation of the SONAS® ultrasound device for the assessment of bilateral cerebral perfusion in subjects with acute stroke

Summary

EudraCT number	2018-001279-19
Trial protocol	DE AT
Global end of trial date	29 December 2019

Results information

Result version number	v1 (current)
This version publication date	25 December 2021
First version publication date	25 December 2021

Trial information

Trial identification

Sponsor protocol code	SONAS2018

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	BURL Concepts, Inc.
Sponsor organisation address	4901 Morena Blvd, suite 703, San Diego, CA 92117, United States,
Public contact	Clinical Trials Information, BURL Concepts, Inc., 001 619277 3702,
Scientific contact	Clinical Trials Information, BURL Concepts, Inc., 001 619277 3702,

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 February 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the safety and feasibility of detecting acoustic signals related to blood supply in subjects with acute stroke by using the SONAS® device.

Protection of trial subjects:

The clinical investigation was conducted in compliance with the Declaration of Helsinki, clinical investigation plan, EN ISO 14155:2011, ICH GCP, and any conditions of approval imposed by the reviewing ethics committee, competent authority and/or local institution.
Only subjects with acute stroke meeting all inclusion criteria and none of the exclusion criteria had to be entered in the clinical investigation. All subjects were free to withdraw at any time and for any reasons. Subjects underwent SONAS® testing only after receiving routine clinical care for stroke management (including cerebral imaging computed tomography [cCT] or cerebral magnetic resonance imaging [cMRI]). All subjects were carefully monitored for the occurrence of adverse events (AEs) from the start of any investigation-related procedure until 72 hours after the second SONAS® testing.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 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	Germany: 20
Worldwide total number of subjects	20
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)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	7
From 65 to 84 years	10
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Male and female subjects aged at least 18 years with acute stroke diagnosed within 24 hours of symptoms onset and assessed intracranial arteria circulation by cMRI or cCCT were recruited in 1 center in Germany. The first subject signed the informed consent form on 01-Apr-2019 and the last subject on 25-Dec-2019.

Pre-assignment

Screening details:

20 subjects signed the informed consent. The SONAS® test was performed at least once on all subjects using the SONAS® device.

Period 1

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

Arms

Arm title	SONAS® test

Arm description:

Subjects with 2 SONAS® tests using the SONAS® device 24 (±4) hours apart.

Arm type	Experimental
Investigational medicinal product name	SONAS® device
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pharmaceutical dose form not applicable
Routes of administration	External use

Dosage and administration details:

2 SONAS® tests using the SONAS® device were performed 24 (±4) hours apart.

Number of subjects in period 1	SONAS® test
Started	20
Completed	18
Not completed	2
Adverse event, serious fatal	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	SONAS® test
Reporting group description:	
Subjects with 2 SONAS® tests using the SONAS® device 24 (±4) hours apart.	

Reporting group values	SONAS® test	Total	
Number of subjects	20	20	
Age categorical Units: Subjects			
Adults (≥18 years)	20	20	
Age continuous Units: years			
median	80.5		
full range (min-max)	44 to 91	-	
Gender categorical Units: Subjects			
Female	14	14	
Male	6	6	
Race Units: Subjects			
White	20	20	

End points

End points reporting groups

Reporting group title	SONAS® test

Reporting group description:

Subjects with 2 SONAS® tests using the SONAS® device 24 (±4) hours apart.

Primary: Diagnostic performance results of SONAS® at first assessment

End point title	Diagnostic performance results of SONAS® at first

End point description:

The endpoint consists of the following parameters:
- Diagnostic accuracy: percentage of subjects in whom the SONAS® assessment result matched the reference standard assessment
- Sensitivity: percentage of subjects positive per SONAS®, among those subjects with confirmed strokes per the reference standard
- Specificity: percentage of subjects negative per SONAS®, among those subjects confirmed as not having a stroke per the reference standard

End point type	Primary

End point timeframe:

At Day 0 (first SONAS® test).

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: No statistical analysis for this end point was done.

End point values	SONAS® test			
Subject group type	Reporting group			
Number of subjects analysed	17[2]			
Units: Percentage				
number (not applicable)				
Diagnostic accuracy (SONAS® and reference match)	88.2			
Sensitivity (positive per SONAS®)	92.9			
Specificity (negative per SONAS®)	66.7			

Notes:

[2] - 3 subjects were excluded from analysis: N=1 met an exclusion criterion, N=2 had no usable data.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the start of any investigation-related procedure until 72 hours after the second SONAS® testing.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	SONAS® test

Reporting group description: -

Serious adverse events	SONAS® test		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 20 (35.00%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events	6		
Nervous system disorders			
Brain oedema			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Sudden cardiac death			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		

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

Non-serious adverse events	SONAS® test		
Total subjects affected by non-serious adverse events subjects affected / exposed	17 / 20 (85.00%)		
Vascular disorders Arteriosclerosis subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Haematoma subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Hypertension subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3		
Peripheral embolism subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
General disorders and administration site conditions Pain subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Respiratory, thoracic and mediastinal disorders Pleural effusion subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Psychiatric disorders Delirium subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3		
Sleep disorder			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Blood urine present			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Inflammatory marker increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fibula fracture			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Joint dislocation			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Cardiac failure			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nervous system disorders			
Carotid artery thrombosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Intracranial aneurysm			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

Monoparesis subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 3 / 20 (15.00%) 3 1 / 20 (5.00%) 1		
Skin and subcutaneous tissue disorders Decubitus ulcer subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		
Infections and infestations Corneal infection subjects affected / exposed occurrences (all) Pneumonia subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 10 / 20 (50.00%) 10 1 / 20 (5.00%) 1		
Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all) Type 2 diabetes mellitus	 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		

subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 July 2019	Changes to version 3.0 (26-Nov-2018): - All components and subcomponents of the SONAS® system according to the investigator's brochure were described. - Software version 1.12 was to be used for the SONAS® operating unit. - Inclusion criterion no. 3 was adapted. The required NIHSS score was reduced from ≥10 to ≥6, because neurological deficits may develop in a delayed manner, i.e. symptoms may be mild at admission despite a later proven vascular occlusion. - The targeted study population was extended from "subjects with acute large vessel occlusion stroke" to "subjects with acute stroke", because in some subjects with severe neurological deficits, vascular occlusion cannot be proven anymore at admission (e.g. due to spontaneous recanalization). The requirement for a confirmed occlusion was removed in inclusion criterion no. 5. - If an MRI or CT is performed as part of the routine clinical practice at 24 hours, images were to be collected. - It was clarified that one SONAS® application may include a repeat test immediately after the first test to improve the data analysis if it does not jeopardize the subject's health according to the investigator's judgement. - If the subject was able to give consent but was unable to sign the consent form in person due to a physical disability, the subject's willingness to participate in the study may be confirmed by a witness.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported