Clinical trial results:
A single blind, placebo controlled, three period, chronic dosing, multicentre, exploratory study to evaluate the effects of Nacystelyn (20 mg BID and 40 mg BID) on Functional Respiratory Imaging (FRI) parameters in subjects with moderate to severe COPD

Summary

EudraCT number	2019-001160-29
Trial protocol	BE
Global end of trial date	20 August 2020

Results information

Result version number	v1 (current)
This version publication date	08 August 2021
First version publication date	08 August 2021

Trial information

Trial identification

Sponsor protocol code	NAL-II-19-1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Laboratoires SMB S.A.
Sponsor organisation address	rue de la Pastorale, 26-28, Brussels, Belgium, 1080
Public contact	CLINICAL DEPARTMENT, LABORATOIRES SMB S.A, 32 2411 48 28, dptclinique@smb.be
Scientific contact	CLINICAL DEPARTMENT, LABORATOIRES SMB S.A, 32 2411 48 28, dptclinique@smb.be

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	13 January 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 August 2020
Global end of trial reached?	Yes
Global end of trial date	20 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the effect of chronic dosing of different doses of NAL on changes in airway geometry with Functional Respiratory Imaging (FRI).

Protection of trial subjects:

For this study, no particular measure was taken to protect the trial patients.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 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	Belgium: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	6
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This multicenter study was conducted in three sites in Belgium. The recruitment was adequate to meet the target of enrollment. The study consisted of a pre-screening visit, a screening visit, a run-in period (28 ± 2 days), at least 4 visits during the treatment periods and a follow-up call.

Pre-assignment

Screening details:

- Obtain signed ICF and demo data
- Perform a medical history & physical examination (HEENT and chest)
-Take vital signs
-Review prior/concomitant medications
-Perform urinary pregnancy test
-Review inclusion/exclusion criteria
-Perform spirometry and body plethysmography
-Demonstrate medication inhalation technique
-Complete CRQ-SR

Period 1

Period 1 title	Placebo Nacystelyn bid
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo Nacystelyn
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Inhalation use

Dosage and administration details:

Mannitol 40 mg hard capsules (Placebo)

Number of subjects in period 1	Placebo
Started	16
Completed	15
Not completed	1
Protocol non-compliance	1

Period 2	
Period 2 title	Nacystelyn 20 mg bid
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms	
Arm title	Nacystelyn 20 mg bid
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Nacystelyn 20 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Inhalation use

Dosage and administration details:

Nacystelyn inhalation powder 20 mg hard capsules
One capsule bid.

Number of subjects in period 2	Nacystelyn 20 mg bid
Started	15
Completed	14
Not completed	1
Adverse event, non-fatal	1

Period 3	
Period 3 title	Nacystelyn 40 mg bid
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms	
Arm title	Nacystelyn 40 mg bid
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Nacystelyn 40 mg (2X20 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Inhalation use

Dosage and administration details:

Nacystelyn inhalation powder 20 mg hard capsules

Two capsules bid

Number of subjects in period 3	Nacystelyn 40 mg bid
Started	14
Completed	12
Not completed	2
Consent withdrawn by subject	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups

Reporting group title	Placebo Nacystelyn bid

Reporting group description: -

Reporting group values	Placebo Nacystelyn bid	Total	
Number of subjects	16	16	
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			
arithmetic mean	68.50		
standard deviation	± 7.87	-	
Gender categorical Units: Subjects			
Female	2	2	
Male	14	14	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Nacystelyn 20 mg bid
Reporting group description: -	
Reporting group title	Nacystelyn 40 mg bid
Reporting group description: -	

Primary: Specific airway volume (SiVaw) at TLC

End point title	Specific airway volume (SiVaw) at TLC
End point description:	
End point type	Primary
End point timeframe:	
This parameter was assessed at baseline (Week 0), week 6 and week 18 (for the extended period).	

End point values	Placebo	Nacystelyn 20 mg bid	Nacystelyn 40 mg bid	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	15	12	
Units: ML/L				
arithmetic mean (standard deviation)	1.676 (± 0.970)	1.643 (± 1.668)	1.701 (± 1.452)	

Statistical analyses

Statistical analysis title	Linear mixed effect model
Comparison groups	Placebo v Nacystelyn 20 mg bid v Nacystelyn 40 mg bid
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mixed models analysis

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
The AEs were recorded during the entire study period.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	NAL 20 mg
Reporting group description: -	
Reporting group title	NAL 40 mg
Reporting group description: -	

Serious adverse events	Placebo	NAL 20 mg	NAL 40 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 14 (7.14%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Arterial bypass thrombosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	NAL 20 mg	NAL 40 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 16 (18.75%)	0 / 15 (0.00%)	4 / 14 (28.57%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	1 / 14 (7.14%)
occurrences (all)	2	0	1
Nasal congestion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 March 2020	RATIONALE FOR SUBSTANTIAL AMENDMENT: The primary objective of this study was to assess the effect of chronic dosing of different doses of NAL on changes in airway geometry with Functional Respiratory Imaging (FRI) in COPD patients. According to the protocol V 1.0 dated on 25 April 2019, the study duration was of approximately 6 months for each patients. The study consisted of a pre-screening visit, a screening visit, a run-in period, 4 visits during the treatment periods and a follow-up call. At each of the 4 visits during the treatment period, placebo, NAL 20 mg or NAL 40 mg treatment was provided for a period of 6 weeks +/- 5 days. An interim analysis was scheduled after the first 5 patients and was performed on 04 March 2020. The results of the interim analysis confirmed the good tolerability of the NAL treatments. A trend to improvement regarding the lung volume was observed in favor of the NAL 40 mg treatment. However it seems that 6 weeks would not be enough to confirm this positive trend. The sponsor thought that an additional period of 12 weeks would be needed to reinforce the study results and support the chronic administration of NAL in a future phase 3 study in COPD patients. Therefore an amendment was submitted to extent the third period of the study (NAL 40 mg bid) by 12 additional weeks (2 periods of 6 weeks +/- 5 days). Two additional visits were added to the third study period. At these additional visits, patients received NAL 40 mg treatment bid for a period of 6 weeks +/- 5 days.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported