



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

| 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 (\pm 0.970) | 1.643 (\pm 1.668) | 1.701 (\pm 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 | <p>RATIONALE FOR SUBSTANTIAL AMENDMENT:</p> <p>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.</p> <p>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.</p> <p>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.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported