Clinical trial results:
A randomized, partially blinded, parallel study to evaluate the effects of nacystelyn in combination with isotretinoin in the treatment of recalcitrant acne vulgaris.

Summary

EudraCT number	2020-005270-10
Trial protocol	BG
Global end of trial date	01 September 2022

Results information

Result version number	v1 (current)
This version publication date	16 July 2023
First version publication date	16 July 2023

Trial information

Trial identification

Sponsor protocol code	NALISO-II-20-1

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	26-28, rue de la Pastorale, Brussels, Belgium, 1080
Public contact	Clinical Department, LABORATOIRES SMB S.A., ++32 2 411 48 28, dptclinique@smb.be
Scientific contact	Clinical Department, LABORATOIRES SMB S.A., ++32 2 411 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	07 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2022
Global end of trial reached?	Yes
Global end of trial date	01 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of the nacystelyn in combination with isotretinoin of different concentrations in patients with severe recalcitrant acne vulgaris

Protection of trial subjects:

The study treatment (isotretinoin) was already on the European market and then were well known by the most of participating patients and investigators. Contraceptive measures and pregnancy tests were mandatory for all women of childbearing potential included in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 November 2021
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	Bulgaria: 90
Worldwide total number of subjects	90
EEA total number of subjects	90

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)	35
Adults (18-64 years)	55
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in five sites in Bulgaria. The recruitment was adequate to meet the target of 90 patients. After the screening visit, the patients were randomized in one of the three groups of treatments. The study extended over 20 weeks of treatment followed by a final visit 4 weeks after the last administration of study treatment.

Pre-assignment

Screening details:

Screening details:
- Obtain signed ICF & assent for adolescents
-Obtain demo data
- Perform a medical history & physical examination
-Take vital signs
-Review prior/concomitant medications
-Perform laboratory evaluation & pregnancy test
-Review inclusion/exclusion criteria
-Schedule the randomization visit

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Isotretinoin 0.5 mg/kg/day + Nacystelyn Placebo

Arm description:

Isotretinoin administered orally with food once a day as 10 mg or 20 mg capsules at a stable dose of approximately 0.5 mg/kg/day + Nacystelyn Placebo (2 sachets of placebo) once daily with a glass of water.

Arm type	Active comparator
Investigational medicinal product name	Isotretinoin (EPURIS) + Nacystelyn Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Powder for oral suspension in sachet
Routes of administration	Oral use

Dosage and administration details:

Isotretinoin 0.5 mg/kg/day - oral and Nacystelyn Placebo - oral

Arm title	Isotretinoin 0.5 mg/kg/day + Nacystelyn 2400 mg

Arm description:

Isotretinoin administered orally with food once a day as 10 mg or 20 mg capsules at a stable dose of approximately 0.5 mg/kg/day + Nacystelyn 2400 mg (2 sachets of 1200 mg) once daily with a glass of water.

Arm type	Experimental
Investigational medicinal product name	Isotretinoin (EPURIS) + Nacystelyn 2400 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Powder for oral suspension in sachet
Routes of administration	Oral use

Dosage and administration details:

Isotretinoin 0.5 mg/kg/day - oral and Nacystelyn 2400 mg - oral

Arm title	Isotretinoin 0.25 mg/kg/day + Nacystelyn 2400 mg

Arm description:

Isotretinoin administered orally with food once a day as 10 mg or 20 mg capsules at a stable dose of approximately 0.25 mg/kg/day + Nacystelyn 2400 mg (2 sachets of 1200 mg) once daily with a glass of water.

Arm type	Experimental
Investigational medicinal product name	Isotretinoin (EPURIS) + Nacystelyn 2400 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Powder for oral suspension in sachet
Routes of administration	Oral use

Dosage and administration details:

Isotretinoin 0.25 mg/kg/day - oral and Nacystelyn 2400 mg - oral

Number of subjects in period 1[1]	Isotretinoin 0.5 mg/kg/day + Nacystelyn Placebo	Isotretinoin 0.5 mg/kg/day + Nacystelyn 2400 mg	Isotretinoin 0.25 mg/kg/day + Nacystelyn 2400 mg
Started	28	29	30
Completed	27	29	28
Not completed	1	0	2
Consent withdrawn by subject	1	-	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Yes, indeed, the number of subjects reported in the baseline period is less than initially foreseen. Three patients were excluded from the analysis set because they did not take any study drug unit (one patient was erroneously randomized and directly withdrawn from the study; and two patients decided to withdraw their consent few hours after signature).

Baseline characteristics

Reporting groups	
Reporting group title	Isotretinoin 0.5 mg/kg/day + Nacystelyn Placebo
Reporting group description:	
Isotretinoin administered orally with food once a day as 10 mg or 20 mg capsules at a stable dose of approximately 0.5 mg/kg/day + Nacystelyn Placebo (2 sachets of placebo) once daily with a glass of water.	
Reporting group title	Isotretinoin 0.5 mg/kg/day + Nacystelyn 2400 mg
Reporting group description:	
Isotretinoin administered orally with food once a day as 10 mg or 20 mg capsules at a stable dose of approximately 0.5 mg/kg/day + Nacystelyn 2400 mg (2 sachets of 1200 mg) once daily with a glass of water.	
Reporting group title	Isotretinoin 0.25 mg/kg/day + Nacystelyn 2400 mg
Reporting group description:	
Isotretinoin administered orally with food once a day as 10 mg or 20 mg capsules at a stable dose of approximately 0.25 mg/kg/day + Nacystelyn 2400 mg (2 sachets of 1200 mg) once daily with a glass of water.	

Reporting group values	Isotretinoin 0.5 mg/kg/day + Nacystelyn Placebo	Isotretinoin 0.5 mg/kg/day + Nacystelyn 2400 mg	Isotretinoin 0.25 mg/kg/day + Nacystelyn 2400 mg
Number of subjects	28	29	30
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	13	11	10
Adults (18-64 years)	15	18	20
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	21.7	22.1	21.8
standard deviation	± 8.1	± 8.8	± 9.1
Gender categorical			
Units: Subjects			
Female	17	16	17
Male	11	13	13

Reporting group values	Total		
Number of subjects	87		
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)	34		
Adults (18-64 years)	53		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	50		
Male	37		

End points

End points reporting groups

Reporting group title	Isotretinoin 0.5 mg/kg/day + Nacystelyn Placebo
Reporting group description:	
Isotretinoin administered orally with food once a day as 10 mg or 20 mg capsules at a stable dose of approximately 0.5 mg/kg/day + Nacystelyn Placebo (2 sachets of placebo) once daily with a glass of water.	
Reporting group title	Isotretinoin 0.5 mg/kg/day + Nacystelyn 2400 mg
Reporting group description:	
Isotretinoin administered orally with food once a day as 10 mg or 20 mg capsules at a stable dose of approximately 0.5 mg/kg/day + Nacystelyn 2400 mg (2 sachets of 1200 mg) once daily with a glass of water.	
Reporting group title	Isotretinoin 0.25 mg/kg/day + Nacystelyn 2400 mg
Reporting group description:	
Isotretinoin administered orally with food once a day as 10 mg or 20 mg capsules at a stable dose of approximately 0.25 mg/kg/day + Nacystelyn 2400 mg (2 sachets of 1200 mg) once daily with a glass of water.	

Primary: Relative change from baseline in the total number of nodules (facial and truncal) at week 20.

End point title	Relative change from baseline in the total number of nodules (facial and truncal) at week 20.
End point description:	
End point type	Primary
End point timeframe:	
Baseline and week 20	

End point values	Isotretinoin 0.5 mg/kg/day + Nacystelyn Placebo	Isotretinoin 0.5 mg/kg/day + Nacystelyn 2400 mg	Isotretinoin 0.25 mg/kg/day + Nacystelyn 2400 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	27	28	30	
Units: percentage				
arithmetic mean (standard deviation)	97.7 (± 6.4)	93.0 (± 14.7)	93.0 (± 11.3)	

Statistical analyses

Statistical analysis title	Mixed model
Comparison groups	Isotretinoin 0.25 mg/kg/day + Nacystelyn 2400 mg v Isotretinoin 0.5 mg/kg/day + Nacystelyn Placebo

Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 1-sided
Parameter estimate	Mean difference (final values)
Point estimate	-4.67
Confidence interval	
level	95 %
sides	1-sided
lower limit	-8.8
Variability estimate	Standard error of the mean
Dispersion value	2.46

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	23.0

Reporting groups	
Reporting group title	Isotretinoin 0.5 mg/kg/day + Nacystelyn Placebo
Reporting group description:	
Isotretinoin 0.5 mg/kg/day + Nacystelyn Placebo once a day	
Reporting group title	Isotretinoin 0.5 mg/kg/day + Nacystelyn 2400 mg
Reporting group description:	
Isotretinoin 0.5 mg/kg/day + Nacystelyn 2400 mg once a day	
Reporting group title	Isotretinoin 0.25 mg/kg/day + Nacystelyn 2400 mg
Reporting group description:	
Isotretinoin 0.25 mg/kg/day + Nacystelyn 2400 mg once a day	

Serious adverse events	Isotretinoin 0.5 mg/kg/day + Nacystelyn Placebo	Isotretinoin 0.5 mg/kg/day + Nacystelyn 2400 mg	Isotretinoin 0.25 mg/kg/day + Nacystelyn 2400 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	1 / 29 (3.45%)	0 / 30 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Broken arm (Fractura RLT Dextra)			
subjects affected / exposed	0 / 28 (0.00%)	1 / 29 (3.45%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
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	Isotretinoin 0.5 mg/kg/day + Nacystelyn Placebo	Isotretinoin 0.5 mg/kg/day + Nacystelyn 2400 mg	Isotretinoin 0.25 mg/kg/day + Nacystelyn 2400 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 28 (75.00%)	25 / 29 (86.21%)	22 / 30 (73.33%)
Nervous system disorders			

Headache			
subjects affected / exposed	1 / 28 (3.57%)	4 / 29 (13.79%)	7 / 30 (23.33%)
occurrences (all)	1	14	15
Gastrointestinal disorders			
Chapped lips			
subjects affected / exposed	19 / 28 (67.86%)	19 / 29 (65.52%)	16 / 30 (53.33%)
occurrences (all)	25	21	16
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 29 (0.00%)	2 / 30 (6.67%)
occurrences (all)	1	0	2
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 28 (0.00%)	2 / 29 (6.90%)	3 / 30 (10.00%)
occurrences (all)	0	2	5
Dry skin			
subjects affected / exposed	16 / 28 (57.14%)	12 / 29 (41.38%)	9 / 30 (30.00%)
occurrences (all)	17	15	10
Rash			
subjects affected / exposed	2 / 28 (7.14%)	0 / 29 (0.00%)	1 / 30 (3.33%)
occurrences (all)	2	0	1
Infections and infestations			
Influenza			
subjects affected / exposed	2 / 28 (7.14%)	1 / 29 (3.45%)	2 / 30 (6.67%)
occurrences (all)	3	1	2
COVID-19			
subjects affected / exposed	0 / 28 (0.00%)	1 / 29 (3.45%)	2 / 30 (6.67%)
occurrences (all)	0	1	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported