

**Clinical trial results:**

Multicenter, prospective, randomized, double-blind, two-armed phase IV clinical study for efficacy and safety assessment of two 2% mupirocin containing nasal ointments (MupiroNasal 20mg/g, nasal ointment, Antibiotic-Razgrad AD, Bulgaria as test product and Bactroban 2%, nasal ointment, GlaxoSmithKline, United Kingdom as reference product), applied to the anterior nares in healthy subjects with nasal carriage of Staphylococcus aureus (S. aureus).

Summary

EudraCT number	2018-002913-37
Trial protocol	BG
Global end of trial date	11 November 2019

Results information

Result version number	v1 (current)
This version publication date	19 April 2021
First version publication date	19 April 2021

Trial information**Trial identification**

Sponsor protocol code	MPN-001-07-2018
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Antibiotic-Razgrad AD
Sponsor organisation address	68 "Aprilsko vastanie" blvd., office 201, Razgrad, Bulgaria, 7200
Public contact	Medical and Regulatory Affairs, Antibiotic-Razgrad AD, +359 897967097, bhodzhova@antibiotic.bg
Scientific contact	Medical and Regulatory Affairs, Antibiotic-Razgrad AD, +359 897967097, bhodzhova@antibiotic.bg

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	22 November 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	11 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the efficacy of MupiroNasal 2% nasal ointment in healthy subjects with nasal carriage of *Staphylococcus aureus* (*S. aureus*).
- To compare the efficacy of MupiroNasal 2% nasal ointment with respect to the Reference medicinal product.

Protection of trial subjects:

Protection of trial subjects:

Prior to the start of the study, the study protocol, the informed consent and assent documents, patient instruction sheets, as well as any advertising materials used to recruit patients were submitted to Bulgarian Drug Agency (BDA) and ethics committees for multicenter trials (ECMT). The BDA/ECMTs reviewed all documents and approved required documents. Consistent with both the BDA/ECMT's requirements and all applicable regulations, the Investigators periodically provided study updates to the BDA/ECMT's. A patient provided informed consent, and children signed an approved assent form when appropriate. This study was conducted in accordance with Good Clinical Practices (GCP) and the ethical principles that have their origins in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 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	Bulgaria: 258
Worldwide total number of subjects	258
EEA total number of subjects	258

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)	240
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 4 study centers located in Bulgaria. Patients were recruited to cover the age range from 18-75 years.

Pre-assignment

Screening details:

The study population consisted of healthy adult subject, male or female, for whom the carriage of *S. aureus* has been established.

Screening Visit – part A

- Medical history;
- Medical examination;
- Microbiological swab – both nares

Screening Visit – part B

- Medical history;
- Medical examination;
- Microbiological swab – both nares;

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

Blinding implementation details:

This design is chosen in order to eliminate any potential influence of the knowledge (by either the investigator or the participant) of the treatment used on the compliance to the study procedures or the reported results.

Arms

Are arms mutually exclusive?	Yes
Arm title	Test arm

Arm description:

MupiroNasal 20 mg/g nasal ointment, Antibiotic-Razgrad AD, Bulgaria, Batch N° 403718; Expiry date: 05.2021

Arm type	Experimental
Investigational medicinal product name	MupiroNasal 20 mg/g nasal ointment, Antibiotic-Razgrad AD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal ointment
Routes of administration	Intranasal use

Dosage and administration details:

Selection of doses to be administered - during the study the dose were as per the information of the SmPC – either of both investigation products (test or reference according to the randomization scheme) were applied for a five-day period, two applications daily.

The subjects performed the therapy by themselves. A small amount of the ointment about the size of a match head was placed on the little finger and applied to the inside of each nostril. The nostrils was closed by pressing the sides of the nose together; this spreads the ointment throughout the nares A whole pack of the IMP was provided to each participant. The storage of the product and its use were in accordance with the approved SmPC.

Arm title	Reference arm
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Arm description:

Bactroban 2% nasal ointment, GlaxoSmithKline, United Kingdom, Batch N° GP7G; Expiry date: 03.2021

Arm type	Experimental
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Investigational medicinal product name	Bactroban 2% nasal ointment, GlaxoSmithKline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal ointment
Routes of administration	Intranasal use

Dosage and administration details:

Selection of doses to be administered - during the study the dose were as per the information of the SmPC – either of both investigation products (test or reference according to the randomization scheme) were applied for a five-day period, two applications daily.

The subjects performed the therapy by themselves. A small amount of the ointment about the size of a match head was placed on the little finger and applied to the inside of each nostril. The nostrils was closed by pressing the sides of the nose together; this spreads the ointment throughout the nares
A whole pack of the IMP was provided to each participant. The storage of the product and its use were in accordance with the approved SmPC.

Number of subjects in period 1	Test arm	Reference arm
Started	129	129
Completed	128	128
Not completed	1	1
Consent withdrawn by subject	1	1

Baseline characteristics

Reporting groups

Reporting group title	Test arm
Reporting group description: MupiroNasal 20 mg/g nasal ointment, Antibiotic-Razgrad AD, Bulgaria, Batch № 403718; Expiry date: 05.2021	
Reporting group title	Reference arm
Reporting group description: Bactroban 2% nasal ointment, GlaxoSmithKline, United Kingdom, Batch № GP7G; Expiry date: 03.2021	

Reporting group values	Test arm	Reference arm	Total
Number of subjects	129	129	258
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)	0	0	0
Adults (18-64 years)	120	120	240
From 65-84 years	9	9	18
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	44.6	44.8	
standard deviation	± 14.2	± 12.9	-
Gender categorical Units: Subjects			
Female	95	92	187
Male	34	37	71

Subject analysis sets

Subject analysis set title	MupiroNasal
Subject analysis set type	Sub-group analysis
Subject analysis set description: MupiroNasal 20mg/g, nasal ointment	
Subject analysis set title	Bactroban
Subject analysis set type	Sub-group analysis
Subject analysis set description: Bactroban 2%, nasal ointment	

Reporting group values	MupiroNasal	Bactroban	
Number of subjects	129	129	

Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	120	120	
From 65-84 years	9	9	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	44.6	44.8	
standard deviation	± 14.2	± 12.9	
Gender categorical			
Units: Subjects			
Female	95	92	
Male	34	37	

End points

End points reporting groups

Reporting group title	Test arm
Reporting group description: MupiroNasal 20 mg/g nasal ointment, Antibiotic-Razgrad AD, Bulgaria, Batch N° 403718; Expiry date: 05.2021	
Reporting group title	Reference arm
Reporting group description: Bactroban 2% nasal ointment, GlaxoSmithKline, United Kingdom, Batch N° GP7G; Expiry date: 03.2021	
Subject analysis set title	MupiroNasal
Subject analysis set type	Sub-group analysis
Subject analysis set description: MupiroNasal 20mg/g, nasal ointment	
Subject analysis set title	Bactroban
Subject analysis set type	Sub-group analysis
Subject analysis set description: Bactroban 2%, nasal ointment	

Primary: Apparent Eradication of Nasal Carriage of SA (measured as cure rate, i.e. number of cured subjects in each treatment group)

End point title	Apparent Eradication of Nasal Carriage of SA (measured as cure rate, i.e. number of cured subjects in each treatment group)
End point description:	
End point type	Primary
End point timeframe: Five day treatment period and follow-up 5 days after the end of the treatment.	

End point values	Test arm	Reference arm	MupiroNasal	Bactroban
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	129	129	129	129
Units: Subjects	129	129	129	129

Statistical analyses

Statistical analysis title	Distribution of Staphylococcus Aureus
Comparison groups	MupiroNasal v Bactroban
Number of subjects included in analysis	258
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
P-value	= 0.8019 ^[2]
Method	Fisher exact
Parameter estimate	Mean difference (final values)
Point estimate	-0.1

Confidence interval	
level	95 %
sides	1-sided
lower limit	-0.2
Variability estimate	Standard error of the mean

Notes:

[1] - For both populations (PP and mITT) the criterion for non-inferiority is satisfied. So, decision can be made that the test product (MupiroNasal 20mg/g, nasal ointment, Antibiotic-Razgrad AD, Bulgaria) is noninferior than the reference product (Bactroban 2%, nasal ointment, GlaxoSmithKline, United Kingdom).

[2] - Avalfinal MB Result at Last Visit

Secondary: Number of Subjects with Adverse Events

End point title	Number of Subjects with Adverse Events
End point description:	
End point type	Secondary
End point timeframe:	
Complete study period.	

End point values	MupiroNasal	Bactroban		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	129	129		
Units: Subjects	129	129		

Statistical analyses

Statistical analysis title	Frequencies of adverse events
Statistical analysis description:	
Frequencies of adverse events by arm are compared.	
Comparison groups	MupiroNasal v Bactroban
Number of subjects included in analysis	258
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.095
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The Number of Subjects With Adverse Events and Changes in Vital Signs and Routine Haematology, Clinical Chemistry and Urinalysis Tests Assessed Over the Five Day Treatment Period and Follow-up 5 days after the end of the treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	16

Reporting groups

Reporting group title	All participants
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Reporting group description: -

Serious adverse events	All participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 258 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	All participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 258 (1.16%)		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 258 (1.16%)		
occurrences (all)	3		
Migraine			
subjects affected / exposed	3 / 258 (1.16%)		
occurrences (all)	3		
Immune system disorders			
Allergic reaction to excipient			
subjects affected / exposed	3 / 258 (1.16%)		
occurrences (all)	3		

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