# 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 |

**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 mulricenter 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 № 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 |

Arm description:

Bactroban 2% nasal ointment, GlaxoSmithKline, United Kingdom, Batch № GP7G; Expiry date: 03.2021

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| 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<br>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<br>Units: years | | | |
| arithmetic mean | 44.6 | 44.8 | |
| standard deviation | ± 14.2 | ± 12.9 | |
| Gender categorical<br>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 № 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 | |
| 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 care rate, i.e. number of cured subjects in each treatment group)

| | |
|---|---|
| End point title | Apparent Eradication of Nasal Carriage of SA (measured as care 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 |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 16 |

### Reporting groups

| | |
|---|---|
| Reporting group title | All participants |

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