Clinical trial results:
A multi-centre, randomized, placebo-controlled, double-blind, parallel-group study investigating safety and efficacy of a sore throat lozenge in the symptomatic treatment of patients with acute pharyngitis.

Summary

EudraCT number	2016-003962-24
Trial protocol	DE
Global end of trial date	03 July 2017

Results information

Result version number	v1 (current)
This version publication date	17 September 2020
First version publication date	17 September 2020
Summary attachment (see zip file)	DoriPha Results 6632-9050-04 (results 6632-9050-04.pdf)

Trial information

Trial identification

Sponsor protocol code	6632-9050-04

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medice Arzneimitel Pütter GmbH & Co. KG
Sponsor organisation address	Kuhloweg 37, Iserlohn, Germany, 58638
Public contact	Medizinische Abteilung, Medice Arzneimitel Pütter GmbH & Co. KG , 0049 023719370, dori@medice.de
Scientific contact	Medizinische Abteilung, Medice Arzneimitel Pütter GmbH & Co. KG , 0049 023719370, dori@medice.de

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	15 November 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 July 2017
Global end of trial reached?	Yes
Global end of trial date	03 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Safety and efficacy of Dorithricin® Halstabletten Classic (lozenges)

Protection of trial subjects:

Each study patient could be withdrawn from the study at any time. There was no detriment for the patient due to the discontinuation. The investigator should have tried to find out the reason for withdrawal, if possible. However, the patient was not obliged to disclose the reason for the withdrawal. The investigator could exclude patients from the study for one of the following reasons:
- Occurrence of inacceptable adverse events (definition: inacceptable according to patient's or investigator´s assessment)
- Change in health conditions that put a patient at risk
- Investigator considered it medically necessary

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 January 2017
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	Germany: 321
Worldwide total number of subjects	321
EEA total number of subjects	321

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)	313
From 65 to 84 years	8

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Overall, 328 adult male or female patients with acute pharyngitis were screened at 17 investigational study sites (centres) in Germany. Seven out of 328 patients (2.1%) failed to meet the inclusion- and/or exclusion criteria (screening failures), and 321 patients (97.9%) were randomized to one of the two treatment groups.

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, Data analyst, Carer, Assessor

Blinding implementation details:

The blinding of the study medication is achieved through the following measures:
- active medication and placebo are identically in appearance, shape, size and taste
- the study medication contains the same batch number and expiry date (traceability is ensured by the randomization list) Patients will be allocated to the respective treatment arm based on the random number on the blisters and the secondary package.

Arms

Are arms mutually exclusive?	Yes
Arm title	triple active combination

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Dorithricin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Lozenge
Routes of administration	Oromucosal use

Dosage and administration details:

The initial dose (2 lozenges simultaneously) was administered at the study site. Patients were instructed to administer at home 1 lozenge at intervals of 2 hours (±15 minutes) up to a maximum of 8 lozenges per day. The number of lozenges taken on Day 0 or Day 3 could be less than 8, depending on the clock time of Visit 1 (Day 0) and Visit 2 (Day 3).

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo lozenge
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Lozenge
Routes of administration	Oromucosal use

Dosage and administration details:

The initial dose (2 lozenges simultaneously) was administered at the study site. Patients were instructed to administer at home 1 lozenge at intervals of 2 hours (±15 minutes) up to a maximum of 8 lozenges per day. The number of lozenges taken on Day 0 or Day 3 could be less than 8, depending on the clock time of Visit 1 (Day 0) and Visit 2 (Day 3).

Number of subjects in period 1	triple active combination	Placebo
Started	160	161
Completed	154	158
Not completed	6	3
Consent withdrawn by subject	2	-
Physician decision	1	1
Adverse event, non-fatal	1	-
Lost to follow-up	2	1
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	triple active combination
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	triple active combination	Placebo	Total
Number of subjects	160	161	321
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	37.4	35.5	
standard deviation	± 14.0	± 13.8	-
Gender categorical Units: Subjects			
Female	97	90	187
Male	63	71	134

End points

End points reporting groups

Reporting group title	triple active combination
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS for the efficacy analyses includes all randomized patients with at least one documented application of trial medication (Dorithricin® or placebo) and post-baseline efficacy data for the primary endpoint (Visit 2). In the case an emergency envelope was opened during the study, this “unblinded” patient would have been excluded from the FAS.

Subject analysis set title	PP
Subject analysis set type	Per protocol

Subject analysis set description:

The PP for the efficacy analyses includes all FAS patients who have no protocol deviations that might have a relevant influence on the assessment of the primary endpoint (major protocol violation). This means, that patients who prematurely discontinued the study due to AE, lack of efficacy or any other reason that could have been associated with lack of efficacy or safety, were also included in the PP if major protocol violation did not occur.

Subject analysis set title	SES
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population described by the SES includes all randomized patients with at least one documented application of study medication (Dorithricin® or placebo) and any post-baseline safety data. The SES was analysed mainly with respect to drug safety.

Primary: percentage of total responders 72 hours p.i.d. (full analysis set)

End point title	percentage of total responders 72 hours p.i.d. (full analysis set)

End point description:

Total Responders: complete resolution of throat pain + difficulty in swallowing 72 hours p.i.d.

End point type	Primary

End point timeframe:

72 hours post initial dose

End point values	triple active combination	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	160		
Units: patient	72	49		

Statistical analyses

Statistical analysis title	analysis of total responder
Comparison groups	triple active combination v Placebo

Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0022
Method	generalized estimation equation
Parameter estimate	difference in Total Responder rates
Point estimate	17.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.8
upper limit	29.7

Secondary: percentage of early responders 48 hours p.i.d. (full analysis set)	
End point title	percentage of early responders 48 hours p.i.d. (full analysis set)
End point description:	
Early Responders (complete resolution of throat pain + difficulty in swallowing 48 hours p.i.d.) and remaining symptom-free	
End point type	Secondary
End point timeframe:	
48 hours p.i.d.	

End point values	triple active combination	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	160		
Units: patients	17	6		

Statistical analyses

Statistical analysis title	analysis of early responder
Comparison groups	triple active combination v Placebo
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0115
Method	generalized estimation equation
Parameter estimate	difference in early responder rates
Point estimate	7.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	22.5

Adverse events

Adverse events information	
Timeframe for reporting adverse events: During the 3 days of investigational treatment with Dorithricin® and placebo (Visit 1 – Visit 2).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	Dorithricin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Dorithricin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 160 (0.63%)	1 / 161 (0.62%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 160 (0.63%)	0 / 161 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Dorithricin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 160 (11.25%)	12 / 161 (7.45%)	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 160 (3.75%)	6 / 161 (3.73%)	
occurrences (all)	8	6	
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	2 / 160 (1.25%)	1 / 161 (0.62%)	
occurrences (all)	2	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 160 (1.25%)	0 / 161 (0.00%)	
occurrences (all)	2	0	
Hypoaesthesia oral			
subjects affected / exposed	2 / 160 (1.25%)	0 / 161 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	3 / 160 (1.88%)	3 / 161 (1.86%)	
occurrences (all)	3	3	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 160 (1.88%)	2 / 161 (1.24%)	
occurrences (all)	3	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 April 2017	Inclusion criterion "pain intensity of ≥8 on a 11-point numeric rating scale" was changed to "pain intensity of ≥7 on a 11-point numeric rating scale".

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30329199