Clinical trial results:
A double-blind, randomized, placebo-controlled, parallel-group study comparing safety and efficacy of Dorithricin® lozenges with placebo in the symptomatic treatment of patients with acute pharyngitis

Summary

EudraCT number	2015-003111-38
Trial protocol	DE
Global end of trial date	23 June 2016

Results information

Result version number	v1 (current)
This version publication date	28 April 2022
First version publication date	28 April 2022

Trial information

Trial identification

Sponsor protocol code	6630-9050-03

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medice Arzneimittel Pütter GmbH & Co. KG
Sponsor organisation address	Kuhloweg 37, Iserlohn, Germany, 58638
Public contact	Medizinische Abteilung, Medice Arzneimittel Pütter GmbH & Co. KG, +49 023719370, dori@medice.de
Scientific contact	Medizinische Abteilung, Medice Arzneimittel Pütter GmbH & Co. KG, +49 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	20 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 June 2016
Global end of trial reached?	Yes
Global end of trial date	23 June 2016
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Each study patient could be withdrawn from the study at any time.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	11 January 2016
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: 300
Worldwide total number of subjects	300
EEA total number of subjects	300

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)	286
From 65 to 84 years	14

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Overall, 311 adult male or female patients with acute pharyngitis were screened at 19 investigational study sites in Germany and gave their written informed consent for participation in this study. Eleven patients (3.5% of 311) were screening failures, and 300 patients 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

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:

Patients of both treatment groups received up to 8 lozenges/day on Day 0, Day 1, Day 2, and Day 3. The number of lozenges taken on Day 0 and Day 3 could be less than 8, depending on the clock time of Visit 1 (Day 0) and Visit 2 (Day 3). At Visit 1 (Day 0), the patients received the study medication and immediately administered an initial dose of 2 lozenges (to be taken all at once). Patients were instructed to administer subsequently 1 lozenge at intervals of 2 hrs (± 15 minutes) up to a maximum of 8 lozenges per day.
The study medication was administered orally. A lozenge was to be sucked slowly until it fully dissolved in the mouth. This might have taken a couple of minutes.
Patients were instructed to administer study medication without interruption from Visit 1 to Visit 2 even if no symptoms of acute pharyngitis were present anymore

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:

Patients of both treatment groups received up to 8 lozenges/day on Day 0, Day 1, Day 2, and Day 3. The number of lozenges taken on Day 0 and Day 3 could be less than 8, depending on the clock time of Visit 1 (Day 0) and Visit 2 (Day 3). At Visit 1 (Day 0), the patients received the study medication and immediately administered an initial dose of 2 lozenges (to be taken all at once). Patients were instructed to administer subsequently 1 lozenge at intervals of 2 hrs (± 15 minutes) up to a maximum of 8 lozenges per day.
The study medication was administered orally. A lozenge was to be sucked slowly until it fully dissolved

in the mouth. This might have taken a couple of minutes. Patients were instructed to administer study medication without interruption from Visit 1 to Visit 2 even if no symptoms of acute pharyngitis were present anymore.

Number of subjects in period 1	triple active combination	Placebo
Started	147	153
Completed	141	148
Not completed	6	5
Adverse event, non-fatal	4	2
Lost to follow-up	1	-
Protocol deviation	1	3

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	147	153	300
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	38.6	39.5	
standard deviation	± 15.1	± 14.9	-
Gender categorical Units: Subjects			
Female	88	99	187
Male	59	54	113

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. Patients whose emergency envelopes were opened during the trial were excluded from the FAS.

Primary: percentage of patients with complete resolution of throat pain and difficulty in swallowing 48hrs and 78 hrs after first application

End point title	percentage of patients with complete resolution of throat pain and difficulty in swallowing 48hrs and 78 hrs after first application

End point description:

The primary endpoint variable was defined as the percentage of patients with complete resolution of throat pain and difficulty in swallowing 48 hrs and 72 hrs after first application of treatment. A complete resolution of throat pain and difficulty in swallowing was defined as complete disappearance of both pharyngitis symptoms with no subsequent reoccurrence of throat pain and difficulty in swallowing up to study end based on patient diary data.

End point type	Primary

End point timeframe:

The primary endpoint variable was defined as the percentage of patients with complete resolution of throat pain and difficulty in swallowing 48 hrs and 72 hrs after first application of treatment.

End point values	triple active combination	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	153		
Units: patients	55	58		

Statistical analyses

Statistical analysis title	complete resolution of throat pain and difficulty
Comparison groups	triple active combination v Placebo
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9101
Method	repeated measurement model (GEE)
Parameter estimate	Difference between groups (%)
Point estimate	-0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.1
upper limit	10

Secondary: percentage of patients with complete resolution of throat pain and difficulty in swallowing 48hrs after first applikation

End point title	percentage of patients with complete resolution of throat pain and difficulty in swallowing 48hrs after first applikation

End point description:

End point type	Secondary

End point timeframe:

48 hrs after first application of treatment

End point values	triple active combination	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	153		
Units: patients	33	39		

Statistical analyses

Statistical analysis title	free of symtoms after 48 hrs
Comparison groups	triple active combination v Placebo
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5486
Method	generalized estimation equation
Parameter estimate	Difference between groups (%)
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.3
upper limit	7.3

Secondary: percentage of patients with complete resolution of throat pain and difficulty in swallowing 72hrs after first applikation

End point title	percentage of patients with complete resolution of throat pain

	and difficulty in swallowing 72hrs after first applikation

End point description:

End point type	Secondary

End point timeframe:

72 hrs after first application of treatment

End point values	triple active combination	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	153		
Units: patients	86	86		

Statistical analyses

Statistical analysis title	free of symtoms after 72 hrs
Comparison groups	Placebo v triple active combination
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6383
Method	generalized estimation equation
Parameter estimate	Difference between groups (%)
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9
upper limit	13.08

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were documented by the investigator at each visit (Visit 1 and Visit 2). Additionally, patients were asked to document in the paper-based diary (before the administration of the last lozenge on Day 0, Day 1, Day 2, and Day 3).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Dorithrcin
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	Dorithrcin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 147 (0.00%)	0 / 153 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Dorithrcin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 147 (12.93%)	17 / 153 (11.11%)	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 147 (2.04%)	7 / 153 (4.58%)	
occurrences (all)	3	7	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 147 (2.04%)	2 / 153 (1.31%)	
occurrences (all)	3	2	
Nausea			
subjects affected / exposed	2 / 147 (1.36%)	0 / 153 (0.00%)	
occurrences (all)	2	0	

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 147 (3.40%)	3 / 153 (1.96%)	
occurrences (all)	6	3	
Dysphonia			
subjects affected / exposed	2 / 147 (1.36%)	0 / 153 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Tonsillitis			
subjects affected / exposed	2 / 147 (1.36%)	3 / 153 (1.96%)	
occurrences (all)	2	3	
Rhinitis			
subjects affected / exposed	2 / 147 (1.36%)	3 / 153 (1.96%)	
occurrences (all)	2	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