



Clinical trial results:

Phase IV study comparing the efficacy and safety of an alcohol-free formulation of 0.15% benzydamine hydrochloride spray and benzydamine hydrochloride 3mg lozenges in paediatric patients (6-12 years) with sore throat.

Summary

EudraCT number	2022-003285-20
Trial protocol	HU BG
Global end of trial date	18 January 2024

Results information

Result version number	v1 (current)
This version publication date	16 April 2025
First version publication date	16 April 2025

Trial information

Trial identification

Sponsor protocol code	030(Z)MD22061
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Angelini Pharma S.p.A.
Sponsor organisation address	Via Amelia 70, Roma, Italy, 00181
Public contact	Study Manager, Angelini Pharma S.p.A., 0039 3472274815, martina.barcaroli@angelinipharma.com
Scientific contact	Study Manager, Angelini Pharma S.p.A., 0039 3472274815, martina.barcaroli@angelinipharma.com

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 January 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the local analgesic effect of benzydamine hydrochloride (spray or lozenges) in reducing sore throat pain at T15 min after a single dose administration to paediatric patients.

Protection of trial subjects:

This trial was conducted in accordance with the study protocol, GCPs, Declaration of Helsinki (including up-to-date versions) and applicable regulatory requirements.
The child participated the study only after parents/legal guardian signature of the ICF and GDPR Consent and (whenever possible) by giving his/her own assent. The Investigator asked to confirm the occurrence of the parents/legal guardian's consent (and child's assent,) to participate to the study and to process personal data by signing the relevant ICF and GDPR Consent , respectively.
Original signed versions of the ICFs, GDPR Consents and Assents available for monitoring and auditing visits at the investigational site.

Background therapy: -

Evidence for comparator:

The purpose of this study was generate new clinical data and update available information on the use of benzydamine in children.
The local analgesic effect in reducing throat pain provided by a single application of benzydamine hydrochloride 3 mg lozenges and benzydamine hydrochloride 0.15 % spray was investigated.

Actual start date of recruitment	16 June 2023
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: 138
Country: Number of subjects enrolled	Hungary: 116
Country: Number of subjects enrolled	Romania: 109
Worldwide total number of subjects	363
EEA total number of subjects	363

Notes:

Subjects enrolled per age group

In utero	0
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Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	343
Adolescents (12-17 years)	20
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 363 subjects, male and female pediatric patients (aged 6-12 years) with sore throat symptoms were enrolled, 185 and 178 in the spray and lozenges groups, respectively.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	363
Number of subjects completed	363

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Test drug: 0.15% Benzydamine hydrochloride spray

Arm description:

The first dose (4 puffs) was administered at the site by the investigator, the subject and parents/legal guardian was instructed to administer the dose of 4 puffs from 2 to 6 times a day until sore throat disappearance or for a maximum of 7 days.

Arm type	Experimental
Investigational medicinal product name	Benzydamine hydrochloride 0.15%, oromucosal spray
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Oromucosal use

Dosage and administration details:

The dose of 4 puffs from 2 to 6 times a day until sore throat disappearance or for a maximum of 7 days. 1 puff is equivalent to 0.255mg of benzydamine hydrochloride, thus the first dose is equivalent to 1.02mg and total daily dose ranges from 2.04mg to 6.12mg benzydamine hydrochloride.

Arm title	Test Comparator: Benzydamine hydrochloride lozenges 3mg
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Arm description:

A single 3mg lozenge of benzydamine hydrochloride was administered at the investigational site.

Arm type	Active comparator
Investigational medicinal product name	Lozenge of benzydamine hydrochloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Lozenge
Routes of administration	Oral use

Dosage and administration details:

Dose: 3mg lozenge of benzydamine hydrochloride was administered. Then, parents will take the drug at home, according to the product's relevant SmPC, 3 times a day for a maximum of 7 days from the first application

Number of subjects in period 1	Test drug: 0.15% Benzydamine hydrochloride spray	Test Comparator: Benzydamine hydrochloride lozenges 3mg
Started	185	178
Completed	185	178

Baseline characteristics

Reporting groups

Reporting group title	Overall
Reporting group description: -	

Reporting group values	Overall	Total	
Number of subjects	363	363	
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)	343	343	
Adolescents (12-17 years)	20	20	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	8.6		
standard deviation	± 1.8	-	
Gender categorical			
Units: Subjects			
Female	170	170	
Male	193	193	

Subject analysis sets

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety analyses were performed on the safety population (SP), which included all randomized subjects who have taken at least one dose of the IMP.

Subject analysis set title	m-ITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All randomized subjects who have taken at least one dose of the IMP and having the T15 min posttreatment efficacy assessment with the WBS score were included in the m-ITT population.

Subject analysis set title	PP Population
Subject analysis set type	Per protocol

Subject analysis set description:

All randomized subjects who have taken at least the first dose of the IMP and having all Day 0 (up to T45 min) WBS score evaluations, with no major protocol violations were included in the PP population

Reporting group values	Safety Population	m-ITT	PP Population
Number of subjects	363	362	347
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)	343	342	328
Adolescents (12-17 years)	20	20	19
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	8.6	8.6	8.6
standard deviation	± 1.8	± 1.8	± 1.8
Gender categorical			
Units: Subjects			
Female	170	169	166
Male	193	193	181

End points

End points reporting groups

Reporting group title	Test drug: 0.15% Benzydamine hydrochloride spray
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Reporting group description:

The first dose (4 puffs) was administered at the site by the investigator, the subject and parents/legal guardian was instructed to administer the dose of 4 puffs from 2 to 6 times a day until sore throat disappearance or for a maximum of 7 days.

Reporting group title	Test Comparator: Benzydamine hydrochloride lozenges 3mg
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Reporting group description:

A single 3mg lozenge of benzydamine hydrochloride was administered at the investigational site.

Subject analysis set title	Safety Population
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Subject analysis set type	Safety analysis
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Subject analysis set description:

The safety analyses were performed on the safety population (SP), which included all randomized subjects who have taken at least one dose of the IMP.

Subject analysis set title	m-ITT
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Subject analysis set type	Modified intention-to-treat
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Subject analysis set description:

All randomized subjects who have taken at least one dose of the IMP and having the T15 min posttreatment efficacy assessment with the WBS score were included in the m-ITT population.

Subject analysis set title	PP Population
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Subject analysis set type	Per protocol
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Subject analysis set description:

All randomized subjects who have taken at least the first dose of the IMP and having all Day 0 (up to T45 min) WBS score evaluations, with no major protocol violations were included in the PP population

Primary: WBS at 15 mins

End point title	WBS at 15 mins
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End point description:

The primary endpoint was the non-inferiority of the test product (defined as the difference between test and reference product 95% CI lower bound of WBS score reduction above 10%) when compared to the reference product with respect to the differences in the percentage of participants who reported a reduction of at least one face (equal to two points) in the WBS score at T15 min after the first application vs. baseline.

End point type	Primary
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End point timeframe:

15 min

End point values	Test drug: 0.15% Benzydamine hydrochloride spray	Test Comparator: Benzydamine hydrochloride lozenges 3mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	178		
Units: Percentage (%)	83	86		

Statistical analyses

Statistical analysis title	Wald 95% CI
Statistical analysis description: Wald 95% CI	
Comparison groups	Test drug: 0.15% Benzydamine hydrochloride spray v Test Comparator: Benzydamine hydrochloride lozenges 3mg
Number of subjects included in analysis	363
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Wald 95% CI
Parameter estimate	95% CI
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.6
upper limit	3.5

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Subjects administered with Benzydamine hydrochloride 0.5% spray

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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Reporting groups

Reporting group title	Benzydamine hydrochloride - spray
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Reporting group description: -

Reporting group title	Benzydamine hydrochloride Lozenges 3mg
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Reporting group description: -

Serious adverse events	Benzydamine hydrochloride - spray	Benzydamine hydrochloride Lozenges 3mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 185 (0.00%)	0 / 178 (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: 0.5 %

Non-serious adverse events	Benzydamine hydrochloride - spray	Benzydamine hydrochloride Lozenges 3mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 185 (7.03%)	7 / 178 (3.93%)	
Nervous system disorders			
headache			
subjects affected / exposed	1 / 185 (0.54%)	1 / 178 (0.56%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
application site hypoaesthesia			
subjects affected / exposed	0 / 185 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Fatigue			

subjects affected / exposed occurrences (all)	0 / 185 (0.00%) 0	1 / 178 (0.56%) 1	
Gastrointestinal disorders			
Hypoaesthesia oral			
subjects affected / exposed	1 / 185 (0.54%)	1 / 178 (0.56%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	1 / 185 (0.54%)	0 / 178 (0.00%)	
occurrences (all)	1	0	
Salivary Hypersecretion			
subjects affected / exposed	0 / 185 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 178 (0.00%)	
occurrences (all)	1	0	
Tongue discomfort			
subjects affected / exposed	0 / 185 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	3 / 185 (1.62%)	0 / 178 (0.00%)	
occurrences (all)	3	0	
cough			
subjects affected / exposed	1 / 185 (0.54%)	1 / 178 (0.56%)	
occurrences (all)	1	1	
dysphonia			
subjects affected / exposed	1 / 185 (0.54%)	0 / 178 (0.00%)	
occurrences (all)	1	0	
nasal obstruction			
subjects affected / exposed	0 / 185 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
oropharyngeal discomfort			
subjects affected / exposed	0 / 185 (0.00%)	1 / 178 (0.56%)	
occurrences (all)	0	1	
productive cough			

subjects affected / exposed occurrences (all)	1 / 185 (0.54%) 1	0 / 178 (0.00%) 0	
Skin and subcutaneous tissue disorders drug eruption subjects affected / exposed occurrences (all)	1 / 185 (0.54%) 1	0 / 178 (0.00%) 0	
pruritus subjects affected / exposed occurrences (all)	1 / 185 (0.54%) 1	0 / 178 (0.00%) 0	
Musculoskeletal and connective tissue disorders myalgia subjects affected / exposed occurrences (all)	0 / 185 (0.00%) 0	1 / 178 (0.56%) 1	
Infections and infestations Ear infection subjects affected / exposed occurrences (all)	1 / 185 (0.54%) 1	0 / 178 (0.00%) 0	
rhinitis subjects affected / exposed occurrences (all)	1 / 185 (0.54%) 1	0 / 178 (0.00%) 0	
sinusitis subjects affected / exposed occurrences (all)	0 / 185 (0.00%) 0	1 / 178 (0.56%) 1	
tonsillitis bacterial subjects affected / exposed occurrences (all)	1 / 185 (0.54%) 1	0 / 178 (0.00%) 0	
viral rash subjects affected / exposed occurrences (all)	1 / 185 (0.54%) 1	0 / 178 (0.00%) 0	

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