

**Clinical trial results:****Effectiveness of antitussive, anticholinergic and honey therapy versus usual practice in adults with uncomplicated acute bronchitis [AB4T study]****Summary**

EudraCT number	2018-002563-25
Trial protocol	ES
Global end of trial date	04 October 2021

Results information

Result version number	v1 (current)
This version publication date	29 December 2022
First version publication date	29 December 2022
Summary attachment (see zip file)	Effectiveness of antitussives, anticholinergics, and honey versus usual care in adults with uncomplicated acute bronchitis: a multiarm randomized clinical trial (Family Practice_article_FINAL.pdf)

Trial information**Trial identification**

Sponsor protocol code	IJG-AB4T-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	IDIAP Jordi Gol
Sponsor organisation address	Gran Via de les Corts Catalanes, 587, Barcelona, Spain, 08007
Public contact	Unitat Estudis Medicament, IDIAP Jordi Gol, 34 934824644, agarcia@idiapjgol.org
Scientific contact	Unitat Estudis Medicament, IDIAP Jordi Gol, 34 934824644, agarcia@idiapjgol.org

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	23 June 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 June 2021
Global end of trial reached?	Yes
Global end of trial date	04 October 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the clinical effectiveness of adding 3 symptomatic treatments (dextromethorphan, ipratropium bromide or honey) to normal practice in the reduction of days with moderate-severe cough compared with usual practice

Protection of trial subjects:

Not applicable. Low risk intervention trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 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	Spain: 194
Worldwide total number of subjects	194
EEA total number of subjects	194

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)	146
From 65 to 84 years	45
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients aged 18 years or older, who come to the primary care physician with cough of up to 3 weeks of evolution compatible with an acute bronchitis and who agree to participate in the clinical trial. Patients with suspected mild Covid-19 infection who present with cough as the predominant symptom, with symptoms compatible with acute bronchitis, wi

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	usual care+dextromethorphan

Arm description: -

Arm type	Experimental
Investigational medicinal product name	DEXTROMETHORPHAN HYDROBROMIDE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

15 mg t.i.d.

Arm title	usual care+ipratropium bromide
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	IPRATROPIUM BROMIDE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

20 µg, 2 puffs t.i.d

Arm title	usual care+honey
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Arm description: -

Arm type	Natural treatment
No investigational medicinal product assigned in this arm	

Arm title	usual care
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Arm description: -

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	usual care+dextromethorphan	usual care+ipratropium bromide	usual care+honey
Started	45	53	49
Completed	22	25	26
Not completed	23	28	23
Consent withdrawn by subject	-	-	1
Diary not fulfilled	11	18	14
Adverse event, non-fatal	1	2	-
Lost to follow-up	9	5	8
Lack of efficacy	1	2	-
Protocol deviation	1	1	-

Number of subjects in period 1	usual care
Started	47
Completed	20
Not completed	27
Consent withdrawn by subject	-
Diary not fulfilled	17
Adverse event, non-fatal	-
Lost to follow-up	10
Lack of efficacy	-
Protocol deviation	-

Baseline characteristics

Reporting groups

Reporting group title	usual care+dextromethorphan
Reporting group description: -	
Reporting group title	usual care+ipratropium bromide
Reporting group description: -	
Reporting group title	usual care+honey
Reporting group description: -	
Reporting group title	usual care
Reporting group description: -	

Reporting group values	usual care+dextromethorphan	usual care+ipratropium bromide	usual care+honey
Number of subjects	45	53	49
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	54.0	56.1	50.5
standard deviation	± 17.6	± 14.3	± 15.4
Gender categorical Units: Subjects			
Female	31	37	32
Male	14	16	17

Reporting group values	usual care	Total	
Number of subjects	47	194	
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years)		0 0 0 0 0 0 0	

From 65-84 years		0	
85 years and over		0	

Age continuous			
Units: years			
arithmetic mean	20.5		
standard deviation	± 17.8	-	
Gender categorical			
Units: Subjects			
Female	30	130	
Male	17	64	

End points

End points reporting groups

Reporting group title	usual care+dextromethorphan
Reporting group description: -	
Reporting group title	usual care+ipratropium bromide
Reporting group description: -	
Reporting group title	usual care+honey
Reporting group description: -	
Reporting group title	usual care
Reporting group description: -	

Primary: Day reduction in the duration of moderate-severe cough

End point title	Day reduction in the duration of moderate-severe cough
End point description:	
End point type	Primary
End point timeframe:	
Daily evaluation by the patient's diary, which is collected in the face-to-face visit on day 15 and, if necessary, on the 29th day	

End point values	usual care+dextromethorphan	usual care+ipratropium bromide	usual care+honey	usual care
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	35	30
Units: 1	32	31	32	28

Statistical analyses

Statistical analysis title	Kaplan–Meier survival analysis
Statistical analysis description:	
Kaplan–Meier survival analysis of days with moderate-to-severe cough, that is, time (days) from baseline visit until patient last scored ≥ 3 in either daytime or nocturnal cough in the symptom diary.	
Comparison groups	usual care+dextromethorphan v usual care+ipratropium bromide v usual care+honey v usual care
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 2-3, Day 15 and Day 29

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	usual care+dextromethorphan
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Reporting group description: -

Reporting group title	usual care+ipratropium bromide
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Reporting group description: -

Reporting group title	usual care+honey
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Reporting group description: -

Reporting group title	usual care
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Reporting group description: -

Serious adverse events	usual care+dextromethorphan	usual care+ipratropium bromide	usual care+honey
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 45 (0.00%)	0 / 53 (0.00%)	0 / 49 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	usual care		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 47 (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	usual care+dextromethorphan	usual care+ipratropium bromide	usual care+honey
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 45 (2.22%)	2 / 53 (3.77%)	0 / 49 (0.00%)

Cardiac disorders palpitations subjects affected / exposed occurrences (all)			
	Additional description: slight increasing of cardiac frequency		
	0 / 45 (0.00%) 1	1 / 53 (1.89%) 2	0 / 49 (0.00%) 0
General disorders and administration site conditions headache subjects affected / exposed occurrences (all)			
	1 / 45 (2.22%) 1	0 / 53 (0.00%) 2	0 / 49 (0.00%) 0
Gastrointestinal disorders diarrhoea subjects affected / exposed occurrences (all)			
	0 / 45 (0.00%) 1	1 / 53 (1.89%) 2	0 / 49 (0.00%) 0

Non-serious adverse events	usual care		
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 47 (0.00%)		
Cardiac disorders palpitations subjects affected / exposed occurrences (all)			
	Additional description: slight increasing of cardiac frequency		
	0 / 47 (0.00%) 0		
General disorders and administration site conditions headache subjects affected / exposed occurrences (all)			
	0 / 47 (0.00%) 0		
Gastrointestinal disorders diarrhoea subjects affected / exposed occurrences (all)			
	0 / 47 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 August 2020	Adaptation of the protocol to the current pandemic situation caused by SARS-CoV-2

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
13 March 2020	The outbreak of the COVID-19 pandemic in March 2020. COVID-19 infection, clearly interfered with the normal development of the trial.	18 December 2020

Notes:

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/36239199>