Clinical trial results:
Immediate oral, immediate topical or delayed oral antibiotics for acute otitis media with discharge (the Runny Ear STudy: REST)

Summary

EudraCT number	2017-003635-10
Trial protocol	GB
Global end of trial date	25 September 2020

Results information

Result version number	v1 (current)
This version publication date	25 April 2021
First version publication date	25 April 2021

Trial information

Trial identification

Sponsor protocol code	2814

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Bristol
Sponsor organisation address	Beacon House, Queens Road, Bristol, United Kingdom,
Public contact	Centre for Academic Primary Care, University of Bristol, +44 01179287350, rest-study@bristol.ac.uk
Scientific contact	Centre for Academic Primary Care, University of Bristol, +44 01179287350, rest-study@bristol.ac.uk

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	25 August 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2019
Global end of trial reached?	Yes
Global end of trial date	25 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether either ciprofloxacin 0.3% drops, or delayed oral amoxicillin (clarithromycin if penicillin allergic or other suitable oral antibiotic as chosen by the GP), is non-inferior to current usual care (immediate oral antibiotics) for overall illness duration in children with AOMd presenting to primary care.

Protection of trial subjects:

Details of adverse events were reported via parent completed questionnaire and collected by the study team.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 22
Worldwide total number of subjects	22
EEA total number of subjects	0

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)	4
Children (2-11 years)	16
Adolescents (12-17 years)	2
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening was automated by the TRANSFORM software when a child with ear discharge presented (with parent/guardian) to a recruiting practice. Participant eligibility was then confirmed by the recruiting clinician.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Immediate topical ear drops

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Immediate ciprofloxacin (0.3%) ear drop solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ear drops
Routes of administration	Auricular use

Dosage and administration details:

Immediate ciprofloxacin (0.3%) ear drop solution, four drops given three times a day for 7 days, with an advice sheet on how to administer the ear drops and standardised symptom management advice.

Arm title	Delayed oral amoxicillin

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Delayed oral amoxicillin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Delayed dose-by-age oral amoxicillin suspension given three times a day for 7 days, and an advice sheet containing structured delaying advice and standardised symptom management advice.

Arm title	Immediate oral amoxicillin

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Immediate oral amoxicillin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Immediate dose-by-age oral amoxicillin given three times a day for 7 days, and standardised symptom management advice.

Number of subjects in period 1	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin
Started	10	7	5
Completed	10	7	5

Baseline characteristics

Reporting groups	
Reporting group title	Immediate topical ear drops
Reporting group description: -	
Reporting group title	Delayed oral amoxicillin
Reporting group description: -	
Reporting group title	Immediate oral amoxicillin
Reporting group description: -	

Reporting group values	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin
Number of subjects	10	7	5
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			
median	5	5	6
inter-quartile range (Q1-Q3)	2 to 6	3 to 11	2 to 7
Gender categorical Units: Subjects			
Female	6	2	0
Male	4	5	5

Reporting group values	Total		
Number of subjects	22		
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 median inter-quartile range (Q1-Q3)	- 		
Gender categorical Units: Subjects			
Female	8		
Male	14		

End points

End points reporting groups

Reporting group title	Immediate topical ear drops
Reporting group description: -	
Reporting group title	Delayed oral amoxicillin
Reporting group description: -	
Reporting group title	Immediate oral amoxicillin
Reporting group description: -	

Primary: Primary Outcome: Duration of symptoms

End point title	Primary Outcome: Duration of symptoms[1]
End point description:	
End point type	Primary
End point timeframe:	
From baseline up to 14 days	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The trial was stopped early due to lack of recruitment, as such no formal between group statistical analyses were performed.

End point values	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	6	4	
Units: Days				
median (inter-quartile range (Q1-Q3))	4 (3 to 6)	4 (3 to 7)	6 (4 to 9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Outcome: N with symptoms resolved by day 3

End point title	Secondary Outcome: N with symptoms resolved by day 3
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to 3 days	

End point values	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	6	4	
Units: Participants				
number (not applicable)	3	3	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Outcome: Time to symptoms rated as 'slight problem' or better

End point title	Secondary Outcome: Time to symptoms rated as 'slight problem' or better

End point description:

End point type	Secondary

End point timeframe:

Baseline up to 14 days

End point values	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	6	4	
Units: Days				
median (inter-quartile range (Q1-Q3))	3 (2 to 5)	4 (2 to 6)	3 (3 to 4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Outcome: N with symptoms rated "slight problem" or better by day 3

End point title	Secondary Outcome: N with symptoms rated "slight problem" or better by day 3

End point description:

End point type	Secondary

End point timeframe:

Baseline to day 3

End point values	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	6	4	
Units: Participants				
number (not applicable)	5	3	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Outcome: Duration of moderate or worse pain

End point title	Secondary Outcome: Duration of moderate or worse pain

End point description:

End point type	Secondary

End point timeframe:

Baseline to 14 days

End point values	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	6	4	
Units: Days				
median (inter-quartile range (Q1-Q3))	1 (1 to 3)	2 (1 to 4)	3 (2 to 3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Outcome: Duration of moderate or worse fever

End point title	Secondary Outcome: Duration of moderate or worse fever

End point description:

End point type	Secondary

End point timeframe:

Baseline up to 14 days

End point values	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	6	4	
Units: Days				
median (inter-quartile range (Q1-Q3))	1 (1 to 1)	1 (1 to 1)	1 (1 to 2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Outcome: Duration of moderate or worse ear discharge

End point title	Secondary Outcome: Duration of moderate or worse ear discharge

End point description:

End point type	Secondary

End point timeframe:

Baseline up to 14 days

End point values	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	6	4	
Units: Days				
median (inter-quartile range (Q1-Q3))	2 (1 to 3)	3 (2 to 3)	3 (2 to 3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Outcome: Duration of moderate or worse unwell

End point title	Secondary Outcome: Duration of moderate or worse unwell

End point description:

End point type	Secondary

End point timeframe:

Baseline up to 14 days

End point values	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	6	4	
Units: Days				
median (inter-quartile range (Q1-Q3))	1 (1 to 1)	2 (1 to 3)	2 (2 to 2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Outcome: Duration of moderate or worse sleep

End point title	Secondary Outcome: Duration of moderate or worse sleep

End point description:

End point type	Secondary

End point timeframe:

Baseline up to 14 days.

End point values	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	6	4	
Units: Days				
median (inter-quartile range (Q1-Q3))	1 (1 to 4)	2 (1 to 2)	2 (2 to 2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Outcome: Duration of moderate or worse crying

End point title	Secondary Outcome: Duration of moderate or worse crying

End point description:

End point type	Secondary

End point timeframe:

Baseline up to 14 days

End point values	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	6	4	
Units: Days				
median (inter-quartile range (Q1-Q3))	1 (1 to 3)	2 (1 to 3)	3 (2 to 3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Outcome: Duration of moderate or worse eating/ drinking

End point title	Secondary Outcome: Duration of moderate or worse eating/ drinking

End point description:

End point type	Secondary

End point timeframe:

Baseline up to 14 days.

End point values	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	6	4	
Units: Days				
median (inter-quartile range (Q1-Q3))	1 (1 to 2)	1 (1 to 1)	2 (2 to 2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Outcome: Duration of moderate or worse activities

End point title	Secondary Outcome: Duration of moderate or worse activities

End point description:

End point type	Secondary

End point timeframe:

Baseline up to 14 days

End point values	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	6	4	
Units: Days				
median (inter-quartile range (Q1-Q3))	1 (1 to 1)	2 (1 to 2)	2 (2 to 2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Outcome: Satisfaction with treatment at day 14

End point title	Secondary Outcome: Satisfaction with treatment at day 14

End point description:

End point type	Secondary

End point timeframe:

Day 14

End point values	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	6	4	
Units: Counts				
Extremely satisfied	4	1	2	
Satisfied	3	4	1	
Neither satisfied nor dissatisfied	0	1	0	
Not satisfied	0	0	1	
Extremely dissatisfied	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

At Day 7 participants were asked to report on the previous 7 days. At Day 14 participants were asked to report on the previous 7 days.

Assessment type	Systematic

Dictionary used

Dictionary name	NA
Dictionary version	NA

Reporting groups

Reporting group title	Immediate topical ear drops
Reporting group description: -	
Reporting group title	Delayed oral amoxicillin
Reporting group description: -	
Reporting group title	Immediate oral amoxicillin

Reporting group description: -

Serious adverse events	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Immediate topical ear drops	Delayed oral amoxicillin	Immediate oral amoxicillin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 10 (20.00%)	1 / 7 (14.29%)	1 / 6 (16.67%)
Infections and infestations			
New or worsening symptoms of infection			
subjects affected / exposed	2 / 10 (20.00%)	1 / 7 (14.29%)	1 / 6 (16.67%)
occurrences (all)	2	1	1

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