Clinical trial results:
Optimized treatment for uncomplicated acute appendicitis - active observation with or without antibiotic treatment. A phase IV consecutive clinical treatment trial.

Summary

EudraCT number	2018-001578-71
Trial protocol	SE
Global end of trial date	30 June 2021

Results information

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

Trial information

Trial identification

Sponsor protocol code	App2018 V2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03985514
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Göteborgs Universitet
Sponsor organisation address	Sahlgrenska Universtetssjukhuset/Kirurgi, Göteborg, Sweden, 41345
Public contact	Department of Surgery, Sahlgrenska Universtiy hospital, Göteborgs Universitet, kent.lundholm@surgery.gu.se
Scientific contact	Department of Surgery , Sahlgrenska University Hospital, Göteborgs Universitet, kent.lundholm@surgery.gu.se

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 December 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Antibiotic treatment to unselected patients with acute appendicitis is safe and effective. However, it is unknown to what extent early provision of antibiotic treatment may represent over-treatment due to spontaneous healing of appendix inflammation. The aim of the present study was to evaluate the role of antibiotic treatment versus active in-hospital observation on spontaneous regression of acute appendicitis.

Protection of trial subjects:

The study compares two options for conservative treatment of appendicitis, both of which are approved treatment options in Swedish healthcare.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	01 May 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 126
Worldwide total number of subjects	126
EEA total number of subjects	126

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)	126
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Persons who requested acute medical care at Sahlgrenska University hospital and presented clinical sympoms of acute appendicits were screened according to inclusion/exclusion criteria.
Patients who accepted participation in the study were included and allocated to treatment group by block-randomization.

Pre-assignment

Screening details:

Patients presenting with symptoms of clinical acute appendicitis and fulfilling inclusion criteria.
Age 18-60 years.
Leucocyte blood count < 13,000 µL
C-reactive protein < 60 mg/L

Period 1

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

Blinding implementation details:

The study is a block-randomised study with block alternatives for treatments decided before inclusion.

Arms

Are arms mutually exclusive?	Yes
Arm title	Study group

Arm description:

Active observation with addition of antibiotic treatment. Antibiotics were administered as in-hospital intravenous infusion (24-48 hours) followed by 7-10 days out-hospital oral ab.

Arm type	Active comparator
Investigational medicinal product name	Piperacillin/Tazobactam
Investigational medicinal product code	ATC code: J01CR05
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Piperacillin/Tazobactam (4 g/0.5 g) in 8 -hour intervals, principally attempted for at least 24 hours.

Investigational medicinal product name	Ciprofloxacin
Investigational medicinal product code	ATC code: J01MA2
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

0.5 g twice daily for 7-10 days.

Investigational medicinal product name	Metronidazole
Investigational medicinal product code	ATC code: P01AB01
Other name	Flagyl
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg tree times daily for 7-10 days.

Arm title	Control group

Arm description:	
Active inhospital observation according to standard of care.	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Study group	Control group
Started	69	57
Completed	69	57

Baseline characteristics

Reporting groups	
Reporting group title	Study group
Reporting group description:	
Active observation with addition of antibiotic treatment. Antibiotics were administered as in-hospital intravenous infusion (24-48 hours) followed by 7-10 days out-hospital oral ab.	
Reporting group title	Control group
Reporting group description:	
Active inhospital observation according to standard of care.	

Reporting group values	Study group	Control group	Total
Number of subjects	69	57	126
Age categorical Units: Subjects			
Adults (18-59 years)	69	57	126
Gender categorical Units: Subjects			
Female	35	26	61
Male	34	31	65

End points

End points reporting groups

Reporting group title	Study group
Reporting group description:	
Active observation with addition of antibiotic treatment. Antibiotics were administered as in-hospital intravenous infusion (24-48 hours) followed by 7-10 days out-hospital oral ab.	
Reporting group title	Control group
Reporting group description:	
Active inhospital observation according to standard of care.	

Primary: Treatment failure (need of acute appendectomy)

End point title	Treatment failure (need of acute appendectomy)
End point description:	
Final proportion of patients in each group that needed acute appendectomy, despite inital observation or observation+ antibiotics.	
End point type	Primary
End point timeframe:	
From inclusion to discharge from hospital at initial hospital stay. Information on recurrence rates for entire study period (2018-2021) are reported in the publication. Life-table analysis indicated a 38% benefit for the antibiotic group.	

End point values	Study group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	57		
Units: 1	19	30		

Statistical analyses

Statistical analysis title	Operation at inital hospital stay
Comparison groups	Study group v Control group
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.005
Method	Chi-squared

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From administration to hospital discharge.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups	
Reporting group title	Study group
Reporting group description:	
Active observation with addition of antibiotic treatment. Antibiotics were administered as in-hospital intravenous infusion (24-48 hours) followed py 7-10 days out-hospital oral ab.	

Serious adverse events	Study group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 69 (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	Study group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 69 (1.45%)		
General disorders and administration site conditions			
Skin reaction			
subjects affected / exposed	1 / 69 (1.45%)		
occurrences (all)	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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The summary include results from primary endpoint at hospital discharge. Further information from entire study period is available in the publication.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/38218686