



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 symptoms of acute appendicitis 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 μ L
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 three times daily for 7-10 days.

| | |
|------------------|---------------|
| Arm title | Control group |
|------------------|---------------|

Arm description:

Active in-hospital 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 in-hospital 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 in-hospital 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 initial 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 initial 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 by 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>