



Clinical trial results: Shortened Antibiotic Treatment in Community-Acquired Pneumonia: A Nationwide Danish Randomized Controlled Trial Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2019-000404-15 |
| Trial protocol | DK |
| Global end of trial date | 22 January 2025 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 23 April 2026 |
| First version publication date | 23 April 2026 |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | 34666 |
|-----------------------|-------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04089787 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Thomas Benfield |
| Sponsor organisation address | Kettegaard Alle 30, Hvidovre, Denmark, 2650 |
| Public contact | Simone Bastrup Israelsen, Thomas Benfield, simone.elisabeth.bastrup.israelsen.02@regionh.dk |
| Scientific contact | Simone Bastrup Israelsen, Thomas Benfield, simone.elisabeth.bastrup.israelsen.02@regionh.dk |

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 | 08 April 2025 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 22 January 2025 |
| Global end of trial reached? | Yes |
| Global end of trial date | 22 January 2025 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy and safety of shortened antibiotic treatment duration of community-acquired pneumonia in hospitalized immunocompetent adult patients based on clinical stability criteria in a beta-lactam antibiotic setting

Protection of trial subjects:

The planned investigations and measurements are not expected to exceed usual clinical care. Pain and discomfort in relation to blood samples for adult patients are regarded insignificant. X-ray radiation in relation to initial chest X-ray is considered an acceptable radiation risk, as the approximate dose of a chest X-ray is only 0,05 mSv corresponding to 6 days of natural background radiation in Denmark.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 21 September 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 | Denmark: 395 |
| Worldwide total number of subjects | 395 |
| EEA total number of subjects | 395 |

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) | 106 |
| From 65 to 84 years | 214 |
| 85 years and over | 75 |

Subject disposition

Recruitment

Recruitment details:

Investigators and treating physicians associated to the research project will identify patients eligible for trial inclusion at day 1-4 after hospital admission. Eligible patients will receive verbal and written information on the study, and subsequently be offered participation.

Pre-assignment

Screening details:

Day 1 is defined by the initiation of antimicrobial therapy for CAP during hospitalization. Day 1-4 serves as screening period to determine study eligibility. Eligible patients will be included in the trial from day 1 to day 5 and randomized at day 3, 4 or 5.

Period 1

| | |
|------------------------------|-------------------------------|
| Period 1 title | Intervention (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Data analyst ^[1] |

Blinding implementation details:

The trial had an open-label design, in which participants, treating physicians, and investigators were aware of treatment allocation, while outcome assessors remained blinded.

Arms

| | |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Intervention |

Arm description:

Patients were randomly assigned to receive either a short-course (5 days) of antibiotic treatment (intervention group) or a standard-course (≥ 7 days) of antibiotic treatment (control group). In the intervention group, antibiotic treatment was discontinued after 5 days. Antibiotic type, route, and dosage were left to physician discretion.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | piperacillin/tazobactam |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for dispersion for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

In the intervention group, antibiotic treatment was discontinued after 5 days, whereas in the control group, the duration was determined by the treating physician but had to be at least 7 days. Antibiotic type, route, and dosage were left to physician discretion.

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

Arm description:

Patients were randomly assigned to receive either a short-course (5 days) of antibiotic treatment (intervention group) or a standard-course (≥ 7 days) of antibiotic treatment (control group). In the control group, the duration was determined by the treating physician but had to be at least 7 days. Antibiotic type, route, and dosage were left to physician discretion.

| | |
|---|---------|
| Arm type | Control |
| No investigational medicinal product assigned in this arm | |

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Open-label trial, only outcome assessors remained blinded.

| Number of subjects in period 1 | Intervention | Control |
|---------------------------------------|--------------|---------|
| Started | 198 | 197 |
| Completed | 196 | 197 |
| Not completed | 2 | 0 |
| Consent withdrawn by subject | 2 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Intervention |
|-----------------------|--------------|

Reporting group description:

Patients were randomly assigned to receive either a short-course (5 days) of antibiotic treatment (intervention group) or a standard-course (≥ 7 days) of antibiotic treatment (control group). In the intervention group, antibiotic treatment was discontinued after 5 days. Antibiotic type, route, and dosage were left to physician discretion.

| | |
|-----------------------|---------|
| Reporting group title | Control |
|-----------------------|---------|

Reporting group description:

Patients were randomly assigned to receive either a short-course (5 days) of antibiotic treatment (intervention group) or a standard-course (≥ 7 days) of antibiotic treatment (control group). In the control group, the duration was determined by the treating physician but had to be at least 7 days. Antibiotic type, route, and dosage were left to physician discretion.

| Reporting group values | Intervention | Control | Total |
|---|--------------|----------|-------|
| Number of subjects | 198 | 197 | 395 |
| 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 | 75 | 76 | |
| inter-quartile range (Q1-Q3) | 62 to 84 | 64 to 82 | - |
| Gender categorical Units: Subjects | | | |
| Female | 109 | 102 | 211 |
| Male | 89 | 95 | 184 |

End points

End points reporting groups

| | |
|--|--------------|
| Reporting group title | Intervention |
| Reporting group description: Patients were randomly assigned to receive either a short-course (5 days) of antibiotic treatment (intervention group) or a standard-course (≥ 7 days) of antibiotic treatment (control group). In the intervention group, antibiotic treatment was discontinued after 5 days. Antibiotic type, route, and dosage were left to physician discretion. | |
| Reporting group title | Control |
| Reporting group description: Patients were randomly assigned to receive either a short-course (5 days) of antibiotic treatment (intervention group) or a standard-course (≥ 7 days) of antibiotic treatment (control group). In the control group, the duration was determined by the treating physician but had to be at least 7 days. Antibiotic type, route, and dosage were left to physician discretion. | |

Primary: All-cause mortality

| | |
|--------------------------------|---------------------|
| End point title | All-cause mortality |
| End point description: | |
| End point type | Primary |
| End point timeframe: 90-day | |

| End point values | Intervention | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 196 | 197 | | |
| Units: deaths | 6 | 4 | | |

Statistical analyses

| | |
|---|--------------------------|
| Statistical analysis title | Non-inferiority |
| Comparison groups | Intervention v Control |
| Number of subjects included in analysis | 393 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | absolute risk difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 1-sided |
| lower limit | -6 |

Secondary: Readmission

| | |
|-----------------|-------------|
| End point title | Readmission |
|-----------------|-------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

90-day

| End point values | Intervention | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 196 | 197 | | |
| Units: yes/no | 46 | 42 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Length of hospital stay

| | |
|-----------------|-------------------------|
| End point title | Length of hospital stay |
|-----------------|-------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

90 days

| End point values | Intervention | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 196 | 197 | | |
| Units: days | | | | |
| number (not applicable) | 4.0 | 3.9 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of antibiotic therapy

| | |
|-----------------|--------------------------------|
| End point title | Duration of antibiotic therapy |
|-----------------|--------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

90 days

| End point values | Intervention | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 196 | 197 | | |
| Units: days | | | | |
| number (not applicable) | 5.0 | 7.1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: New antibiotic treatment

| | |
|-----------------|--------------------------|
| End point title | New antibiotic treatment |
|-----------------|--------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

90 days

| End point values | Intervention | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 196 | 197 | | |
| Units: yes/no | 45 | 38 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Follow-up visits

| | |
|-----------------|------------------|
| End point title | Follow-up visits |
|-----------------|------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

90 days

| End point values | Intervention | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 196 | 197 | | |
| Units: yes/no | 54 | 36 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mortality

| | |
|------------------------|-----------|
| End point title | Mortality |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 30 days | |

| End point values | Intervention | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 196 | 197 | | |
| Units: yes/no | 2 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Readmission

| | |
|------------------------|-------------|
| End point title | Readmission |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 30 days | |

| End point values | Intervention | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 196 | 197 | | |
| Units: yes/no | 25 | 18 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

90 days

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|------|
| Dictionary name | None |
|-----------------|------|

| | |
|--------------------|---|
| Dictionary version | 0 |
|--------------------|---|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Intervention |
|-----------------------|--------------|

Reporting group description: -

| | |
|-----------------------|---------|
| Reporting group title | Control |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events | Intervention | Control | |
|--|-------------------|-------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 49 / 196 (25.00%) | 49 / 197 (24.87%) | |
| number of deaths (all causes) | 6 | 4 | |
| number of deaths resulting from adverse events | | | |
| General disorders and administration site conditions | | | |
| Hospital admission/prolonged hospital stay | | | |
| subjects affected / exposed | 49 / 196 (25.00%) | 49 / 197 (24.87%) | |
| occurrences causally related to treatment / all | 5 / 57 | 0 / 72 | |
| deaths causally related to treatment / all | 0 / 6 | 0 / 4 | |

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

| Non-serious adverse events | Intervention | Control | |
|---|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 29 / 196 (14.80%) | 32 / 197 (16.24%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 2 / 197 (1.02%) | |
| occurrences (all) | 0 | 2 | |
| Dizziness | | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 196 (0.51%) 1 | 3 / 197 (1.52%) 3 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 2 / 196 (1.02%) | 4 / 197 (2.03%) | |
| occurrences (all) | 2 | 4 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 197 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 20 / 196 (10.20%) | 23 / 197 (11.68%) | |
| occurrences (all) | 20 | 23 | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 196 (1.53%) | 2 / 197 (1.02%) | |
| occurrences (all) | 3 | 2 | |
| Hepatobiliary disorders | | | |
| Elevated liver enzymes | | | |
| subjects affected / exposed | 2 / 196 (1.02%) | 1 / 197 (0.51%) | |
| occurrences (all) | 2 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Skin rash | | | |
| subjects affected / exposed | 2 / 196 (1.02%) | 1 / 197 (0.51%) | |
| occurrences (all) | 2 | 1 | |
| Renal and urinary disorders | | | |
| Elevated creatinine levels | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 197 (0.00%) | |
| occurrences (all) | 1 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 23 November 2023 | Change in primary outcome from composite of 90-day mortality and readmissions to only 90-day mortality and recalculation of sample size due to change in primary outcome and adjustment of confidence intervals (90% to 95%) in accordance with latest updated guidelines. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported