



Clinical trial results:

Estudio de la eficacia de la administración prolongada de antibióticos betalactámicos frente a la administración intermitente en el tratamiento de la infección causada por microorganismo sensibles pero con concentraciones mínimas inhibitorias altas

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2010-024117-31 |
| Trial protocol | ES |
| Global end of trial date | 10 June 2014 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 25 November 2021 |
| First version publication date | 25 November 2021 |
| Summary attachment (see zip file) | APROVECHA publication (Final report Aprobecha.pdf) |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | APROBECHA |
|-----------------------|-----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Clínica Universidad de Navarra |
| Sponsor organisation address | Avda. Pío XII, 36, Pamplona, Spain, 31008 |
| Public contact | UCEC (ucicec@unav.es), Clínica Universidad de Navarra, 34 948255 400, ucicec@unav.es |
| Scientific contact | UCEC (ucicec@unav.es), Clínica Universidad de Navarra, 34 948255 400, ucicec@unav.es |

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 | 13 May 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 13 May 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 June 2014 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

Comparar los parámetros farmacocinéticos/farmacodinámicos (PK/PD) de los betalactámicos en infusión prolongada con los de betalactámicos en infusión intermitente

Protection of trial subjects:

The patients participating in the study consented after adequate information about the study. After inclusion, they were under the surveillance of the investigated team, among whose members were the infectious diseases area staff of the center, so they continued to receive the assistance that their clinical situation required. No other health protection measures were necessary.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 21 February 2012 |
| 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: 3 |
| Worldwide total number of subjects | 3 |
| EEA total number of subjects | 3 |

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) | 1 |
| From 65 to 84 years | 2 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

3 patients were examined and finally included in the study. All of them gave their written consent to participate in the study. Two of the patients were randomized to receive beta-lactam in the experimental group, while the third patient participated in the control group.

Pre-assignment

Screening details:

Before the treatment was assigned, the presence of an infectious process was verified with the isolation of a microorganism with a MIC close to the reference cut-off point according to the CLSI (1-2 dilutions). In all cases, *Pseudomonas aeruginosa* was isolated in the evaluated samples, with a MIC between 8 and 16 for piperacillin-tazobactam.

Period 1

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

Blinding implementation details:

NA

Arms

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

Arm description:

patients with a beta-lactam antibiotic in intermittent infusion following the classic administration guidelines

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | beta-lactams |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

In all cases, the drug was administered diluted in a volume of 100 ml of physiological saline. Administration according to the classical regimen involves administration of the product as a short 30-minute intravenous infusion.

| | |
|------------------|-----------|
| Arm title | Treatment |
|------------------|-----------|

Arm description:

Experimental arm, patients with a beta-lactam antibiotic in prolonged infusion.

| | |
|--|-----------------|
| Arm type | Experimental |
| Investigational medicinal product name | beta-lactams |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

In all cases, the drug was administered diluted in a volume of 100 ml of physiological saline. La administración prolongada suponía la administración del producto en una infusión de 240 minutos.

| Number of subjects in period 1 | Control | Treatment |
|---------------------------------------|---------|-----------|
| Started | 1 | 2 |
| Completed | 1 | 2 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Treatment |
|-----------------------|-----------|

Reporting group description: -

| Reporting group values | Treatment | Total | |
|------------------------|-----------|-------|--|
| Number of subjects | 3 | 3 | |
| Age categorical | | | |
| Units: Subjects | | | |
| > 18 years | 3 | 3 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 1 | 1 | |
| Male | 2 | 2 | |

End points

End points reporting groups

| | |
|---|-----------|
| Reporting group title | Control |
| Reporting group description: patients with a beta-lactam antibiotic in intermittent infusion following the classic administration guidelines | |
| Reporting group title | Treatment |
| Reporting group description: Experimental arm, patients with a beta-lactam antibiotic in prolonged infusion. | |

Primary: Difference between long infusion and intermittent infusion

| | |
|--|---|
| End point title | Difference between long infusion and intermittent infusion ^[1] |
| End point description: After steady equilibrium was reached, blood samples were drawn to measure beta-lactam concentrations. The extractions were carried out in the stipulated times, obtaining the concentrations (µg / ml) of piperacillin | |
| End point type | Primary |
| End point timeframe: Day of extraaction: Extraction in 30 minutes, 1 hour, 2 hours, 4 hours | |

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: It was not possible to perform any analysis of the results, given the low number of patients included in the study. The data of the three patients are presented in a descriptive way.

| End point values | Control | Treatment | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1 | 2 | | |
| Units: Hours | | | | |
| number (not applicable) | 1 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

30 days

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

Dictionary used

| | |
|-----------------|----|
| Dictionary name | NA |
|-----------------|----|

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

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Treatment |
|-----------------------|-----------|

Reporting group description: -

| Serious adverse events | Treatment | | |
|---|---------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | Treatment | | |
|---|----------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | | |
| Gastrointestinal disorders | | | |
| abdominal pain | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 05 July 2012 | Changes in protocol and patient information sheet |
| 23 April 2013 | Changes in inclusion criteria |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|--------------|-------------------------------|--------------|
| 10 June 2014 | Inability to recruit patients | - |

Notes:

Limitations and caveats

None reported