



## Clinical trial results: Concentration of Meropenem in Plasma and Subcutis in Patients on ECMO Treatment

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-000218-23 |
| Trial protocol           | DK             |
| Global end of trial date | 04 May 2016    |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 14 December 2017 |
| First version publication date | 14 December 2017 |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 131188 |
|-----------------------|--------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Ortopædkirurgisk afdeling, Aarhus Universitetshospital                             |
| Sponsor organisation address | Tage-Hansens Gade 2, Aarhus C, Denmark, 8000                                       |
| Public contact               | Pelle Hanberg, Aarhus University Hospital, 0045 28744852, pellehanberg@hotmail.com |
| Scientific contact           | Pelle Hanberg, Aarhus University Hospital, 0045 28744852, pellehanberg@hotmail.com |

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:

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**Results analysis stage**

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|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 01 September 2017 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 04 May 2016       |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 04 May 2016       |
| Was the trial ended prematurely?                     | No                |

Notes:

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**General information about the trial**

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Main objective of the trial:

The objective of this trial is to assess the penetration of meropenem into subcutis using the pharmacokinetic tool microdialysis. The primary endpoint is the time above the minimal inhibitory concentration (T>MIC). Secondary endpoints are standard pharmacokinetic parameters.

Protection of trial subjects:

Measures to trial subjects a good experience with clinical trials.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 01 April 2015 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | Yes           |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Denmark: 10 |
| Worldwide total number of subjects   | 10          |
| EEA total number of subjects         | 10          |

Notes:

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**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)                      | 8 |
| From 65 to 84 years                       | 2 |
| 85 years and over                         | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Criteria to fulfil: age 18 or above, in treatment with meropenem, ongoing ECMO-treatment (<96 hours since start-up of ECMO-treatment, heavily sedated). Exclusion criteria: allergy to meropenem, pregnancy.

### Period 1

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

### Arms

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | overall trial |
|------------------|---------------|

Arm description:

All subjects recieved either 1,000 or 2,000 milligrams of meropenem. No randomisation.

|  |  |
|--|--|
| Arm type                               | All subjects recieved the same amount of drug                |
| Investigational medicinal product name | meropenem "eberth"   |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Powder and solvent for concentrate for solution for infusion |
| Routes of administration               | Intravenous use  |

Dosage and administration details:

1,000 or 2,000 mg milligram(s) administered over 5 min.

Patient 1, 2, 3, 4, 6, 9, and 10 received 1,000 mg.

Patient 5, 7, and 8 received 2,000 mg.

|                                       |               |
|---------------------------------------|---------------|
| <b>Number of subjects in period 1</b> | overall trial |
| Started                               | 10            |
| Completed                             | 10            |

## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | overall trial |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values                             | overall trial | Total |  |
|--|---------------|-------|--|
| Number of subjects                                 | 10            | 10    |  |
| Age categorical                                    |               |       |  |
| Units: Subjects                                    |               |       |  |
| In utero   | 0             | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                               | 0             | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0             | 0     |  |
| Children (2-11 years)                              | 0             | 0     |  |
| Adolescents (12-17 years)                          | 0             | 0     |  |
| Adults (18-64 years)                               | 8             | 8     |  |
| From 65-84 years                                   | 2             | 2     |  |
| 85 years and over                                  | 0             | 0     |  |
| Gender categorical                                 |               |       |  |
| Units: Subjects                                    |               |       |  |
| Female   | 4             | 4     |  |
| Male   | 6             | 6     |  |

### Subject analysis sets

|                            |               |
|----------------------------|---------------|
| Subject analysis set title | overall trial |
|----------------------------|---------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Concentrations values of meropenem in subcutis and plasma.

| Reporting group values                             | overall trial |  |  |
|--|---------------|--|--|
| Number of subjects                                 | 10            |  |  |
| 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)                               | 8             |  |  |
| From 65-84 years                                   | 2             |  |  |
| 85 years and over                                  | 0             |  |  |

|                    |   |  |  |
|--------------------|---|--|--|
| Gender categorical |   |  |  |
| Units: Subjects    |   |  |  |
| Female             | 4 |  |  |
| Male               | 6 |  |  |

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## End points

### End points reporting groups

|  |               |
|--|---------------|
| Reporting group title  | overall trial |
| Reporting group description:<br>All subjects recieved either 1,000 or 2,000 milligrams of meropenem. No randomisation. |               |
| Subject analysis set title   | overall trial |
| Subject analysis set type  | Full analysis |
| Subject analysis set description:<br>Concentrations values of meropenem in subcutis and plasma.                        |               |

### Primary: overall trial

|   |                              |
|---|------------------------------|
| End point title   | overall trial <sup>[1]</sup> |
| End point description:<br>concentrations in milligrams/litre at the following points:<br>subcutis: 7.5 min, 22.5 min, 37.5 min, 52.5 min, 75 min, 105 min, 135 min, 165 min, 195 min, 225 min, 285 min, 330 min, 390 min, 450 min.<br>Plasma: 10 min, 20 min, 30 min, 45 min, 60 min, 120 min, 180 min, 240 min, 480 min. Furthermore, two blood samples were collected on day 2, 4, and 6 at time 60 min and 480 min after the second meropenem dose administrated that day. |                              |
| End point type  | Primary                      |
| End point timeframe:<br>from time 0 to day 6  |                              |

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: Under "Charts" the full dataset has been uploaded as a PDF-file. All measured meropenem values from subcutis and plasma (in milligrams/L) from all the patients are included in the file. With this dataset, people can make their own statistical analyses.

| End point values            | overall trial   | overall trial        |  |  |
|-----------------------------|-----------------|----------------------|--|--|
| Subject group type          | Reporting group | Subject analysis set |  |  |
| Number of subjects analysed | 10              | 10                   |  |  |
| Units: milligram(s)/litre   |                 |                      |  |  |
| number (not applicable)     | 10              | 10                   |  |  |

|                                   |  |
|-----------------------------------|--|
| <b>Attachments (see zip file)</b> | Patient meropenem concentrations/Patient meropenem |
|-----------------------------------|--|

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

from placement of the microdialysis catheter until the last collected blood sample at day 6.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |               |
|-----------------|---------------|
| Dictionary name | produktresume |
|-----------------|---------------|

|                    |            |
|--------------------|------------|
| Dictionary version | 20.okt2014 |
|--------------------|------------|

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | overall trial |
|-----------------------|---------------|

Reporting group description:

All subjects recieved either 1,000 or 2,000 milligrams of meropenem. No randomisation.

| Serious adverse events                            | overall trial  |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 0 / 10 (0.00%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    | 0              |  |  |

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

| Non-serious adverse events                            | overall trial  |  |  |
|---|----------------|--|--|
| Total subjects affected by non-serious adverse events |                |  |  |
| subjects affected / exposed                           | 0 / 10 (0.00%) |  |  |

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: We had no non-serious adverse event in this trial.

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported