



## Clinical trial results: DEXMEDETOMIDINE FOR PERIPHERAL NERVE BLOCKADE: A DOSE-FINDING STUDY IN VOLUNTEERS

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2013-003790-10   |
| Trial protocol           | AT               |
| Global end of trial date | 24 December 2013 |

### Results information

|                                   |  |
|-----------------------------------|--|
| Result version number             | v1 (current)   |
| This version publication date     | 25 February 2016   |
| First version publication date    | 25 February 2016   |
| Summary attachment (see zip file) | Publication_EudraCT 2013-003790-10 (Publication_ EudraCT 2013-003790-10.pdf) |

### Trial information

#### Trial identification

|                       |     |
|-----------------------|-----|
| Sponsor protocol code | 1.0 |
|-----------------------|-----|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Medical University of Vienna   |
| Sponsor organisation address | Währinger Gürtel 18-20, Vienna, Austria, 1090  |
| Public contact               | Maya Keplinger, Medical University of Vienna, 0043 1404004100, maya.keplinger@meduniwien.ac.at |
| Scientific contact           | Maya Keplinger, Medical University of Vienna, 0043 1404004100, maya.keplinger@meduniwien.ac.at |

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**

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 18 February 2015 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 24 December 2013 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 24 December 2013 |
| Was the trial ended prematurely?                     | No               |

Notes:

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**General information about the trial**

Main objective of the trial:

Duration of sensory block of the ulnar nerve

Protection of trial subjects:

Subject were during the trial continuously under the supervision of a physician or an experienced nurse.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 25 November 2013 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Austria: 24 |
| Worldwide total number of subjects   | 24          |
| EEA total number of subjects         | 24          |

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)                      | 24 |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Subjects were recruited by use of the data base of the Clinical Pharmacology, Medical University Vienna.

### Pre-assignment

Screening details:

Check of the In- and Exclusion criteria, Physical examination, Vital signs, Laboratory assessment

### Pre-assignment period milestones

|                              |    |
|------------------------------|----|
| Number of subjects started   | 24 |
| Number of subjects completed | 24 |

### Period 1

|                              |                                     |
|------------------------------|-------------------------------------|
| Period 1 title               | overall trial (overall period)      |
| Is this the baseline period? | Yes                                 |
| Allocation method            | Randomised - controlled             |
| Blinding used                | Double blind                        |
| Roles blinded                | Subject, Investigator, Data analyst |

Blinding implementation details:

The study drugs will be prepared by a study nurse outside the area where the blocks are performed. Both the anaesthetist and the volunteers are not informed about the adjuvants for LA for ulnar nerve blockade. All sensory tests will be performed by a study physician not otherwise involved in the study.

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Group R |

Arm description:

Group R: 3 ml ropivacaine without adjuvants

|  |                        |
|--|------------------------|
| Arm type                               | active control         |
| Investigational medicinal product name | Ropivacaine            |
| Investigational medicinal product code | N01BB09                |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Perineural use         |

Dosage and administration details:

Administration of 22.5mg Ropivacaine perineural as single dose

|                  |            |
|------------------|------------|
| <b>Arm title</b> | Group RD50 |
|------------------|------------|

Arm description:

Group RD50: 22.5 mg ropivacaine mixed with 50 µg dexmedetomidine

|  |                        |
|--|------------------------|
| Arm type                               | Active comparator      |
| Investigational medicinal product name | Ropivacaine            |
| Investigational medicinal product code | N01BB09                |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Perineural use         |

Dosage and administration details:

Administration of 22.5 mg ropivacaine mixed with 50 µg dexmedetomidine perineural as a single dose

|  |                                 |
|--|---------------------------------|
| Investigational medicinal product name | Dexmedetomidine                 |
| Investigational medicinal product code | 29332990                        |
| Other name                             | Dexdor                          |
| Pharmaceutical forms                   | Solution for injection/infusion |
| Routes of administration               | Perineural use                  |

Dosage and administration details:

Administration of 22.5 mg ropivacaine mixed with 50 µg dexmedetomidine perineural as a single dose

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | Group RD100 |
|------------------|-------------|

Arm description:

Group RD100: 22.5 mg ropivacaine mixed with 100 µg dexmedetomidine

|  |                        |
|--|------------------------|
| Arm type                               | Active comparator      |
| Investigational medicinal product name | Ropivacaine            |
| Investigational medicinal product code | N01BB09                |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Perineural use         |

Dosage and administration details:

Administration of 22.5 mg ropivacaine mixed with 100 µg dexmedetomidine perineural as a single dose

|  |                                 |
|--|---------------------------------|
| Investigational medicinal product name | Dexmedetomidine                 |
| Investigational medicinal product code | 29332990                        |
| Other name                             | Dexdor                          |
| Pharmaceutical forms                   | Solution for injection/infusion |
| Routes of administration               | Perineural use                  |

Dosage and administration details:

Administration of 22.5 mg ropivacaine mixed with 100 µg dexmedetomidine perineural as a single dose

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | Group RD150 |
|------------------|-------------|

Arm description:

Group RD150: 22.5 mg ropivacaine mixed with 150 µg dexmedetomidine

|  |                        |
|--|------------------------|
| Arm type                               | Active comparator      |
| Investigational medicinal product name | Ropivacaine            |
| Investigational medicinal product code | N01BB09                |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Perineural use         |

Dosage and administration details:

Administration of 22.5 mg ropivacaine mixed with 150 µg dexmedetomidine perineural as a single dose

|  |                                 |
|--|---------------------------------|
| Investigational medicinal product name | Dexmedetomidine                 |
| Investigational medicinal product code | 29332990                        |
| Other name                             | Dexdor                          |
| Pharmaceutical forms                   | Solution for injection/infusion |
| Routes of administration               | Perineural use                  |

Dosage and administration details:

Administration of 22.5 mg ropivacaine mixed with 150 µg dexmedetomidine perineural as a single dose

| <b>Number of subjects in period 1</b> | Group R | Group RD50 | Group RD100 |
|---------------------------------------|---------|------------|-------------|
| Started                               | 6       | 6          | 6           |
| Completed                             | 6       | 6          | 6           |

| <b>Number of subjects in period 1</b> | Group RD150 |
|---------------------------------------|-------------|
| Started                               | 6           |
| Completed                             | 6           |

## Baseline characteristics

### Reporting groups

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

Reporting group description: -

| Reporting group values                             | overall trial | Total |  |
|--|---------------|-------|--|
| Number of subjects                                 | 24            | 24    |  |
| Age categorical                                    |               |       |  |
| 18 to 45 years of age                              |               |       |  |
| 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)                               | 24            | 24    |  |
| From 65-84 years                                   | 0             | 0     |  |
| 85 years and over                                  | 0             | 0     |  |
| Age continuous                                     |               |       |  |
| 18 to 45   |               |       |  |
| Units: years                                       |               |       |  |
| arithmetic mean                                    | 0             |       |  |
| standard deviation                                 | ± 24          | -     |  |
| Gender categorical                                 |               |       |  |
| Units: Subjects                                    |               |       |  |
| Female   | 0             | 0     |  |
| Male   | 24            | 24    |  |

## End points

### End points reporting groups

|  |              |
|--|--------------|
| Reporting group title  | Group R      |
| Reporting group description:                                       |              |
| Group R: 3 ml ropivacaine without adjuvants                        |              |
| Reporting group title  | Group RD50   |
| Reporting group description:                                       |              |
| Group RD50: 22.5 mg ropivacaine mixed with 50 µg dexmedetomidine   |              |
| Reporting group title  | Group RD100  |
| Reporting group description:                                       |              |
| Group RD100: 22.5 mg ropivacaine mixed with 100 µg dexmedetomidine |              |
| Reporting group title  | Group RD150  |
| Reporting group description:                                       |              |
| Group RD150: 22.5 mg ropivacaine mixed with 150 µg dexmedetomidine |              |
| Subject analysis set title   | main         |
| Subject analysis set type  | Per protocol |
| Subject analysis set description:                                  |              |
| All subjects who were treated according to the protocol            |              |

### Primary: duration of complete sensory block to pinprick and time

|                        |   |
|------------------------|---|
| End point title        | duration of complete sensory block to pinprick and time |
| End point description: |   |
| End point type         | Primary   |
| End point timeframe:   |   |
| full period            |   |

| End point values            | Group R         | Group RD50      | Group RD100     | Group RD150     |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6               | 6               | 6               | 6               |
| Units: hours                |                 |                 |                 |                 |
| number (not applicable)     | 8.7             | 16.4            | 20.4            | 21.2            |

| End point values            | main                 |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed |                      |  |  |  |
| Units: hours                |                      |  |  |  |
| number (not applicable)     | 24                   |  |  |  |

## Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Descriptive evaluation of four different groups  |
| Statistical analysis description:<br>the study was designed as mainly descriptive evaluation of four different study groups. As primary and secondary outcomes consist of time-to-event data, logrank test analyses were performed and the dose-dependency of dexmedetomidine was evaluated with the logrank test for trend. The dose-dependent effects of dexmedetomidine on sedation scores were analysed using the Cuzick trend test. Other data were analysed using a Kruskal–Wallis one-way analysis and unpaired Mann–Whitney U-posthoc test |  |
| Comparison groups  | Group R v Group RD50 v Group RD100 v Group RD150 |
| Number of subjects included in analysis  | 24   |
| Analysis specification   | Pre-specified                                    |
| Analysis type  |  |
| P-value  | < 0.0001   |
| Method   | Mixed models analysis                            |



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:  
from 02.Dec.2013 to 24.Dec.2013

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

### Reporting groups

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

Reporting group description: -

| Serious adverse events                            | overall trial  |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 0 / 24 (0.00%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    |                |  |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events                            | overall trial   |  |  |
|---|---|--|--|
| Total subjects affected by non-serious adverse events |   |  |  |
| subjects affected / exposed                           | 21 / 24 (87.50%)  |  |  |
| Vascular disorders                                    |   |  |  |
| Hypotension   | Additional description: intermittend Hypotension  |  |  |
| subjects affected / exposed                           | 21 / 24 (87.50%)  |  |  |
| occurrences (all)                                     | 21  |  |  |
| Cardiac disorders                                     |   |  |  |
| Sinus bradycardia                                     | Additional description: intermittend Sinus bradycardia                                  |  |  |
| subjects affected / exposed                           | 9 / 24 (37.50%)   |  |  |
| occurrences (all)                                     | 9   |  |  |
| Nervous system disorders                              |   |  |  |
| Hypoaesthesia   | Additional description: Hypoaesthesia at nerv block site after the end of the study day |  |  |
| subjects affected / exposed                           | 2 / 24 (8.33%)  |  |  |
| occurrences (all)                                     | 2   |  |  |
| Headache  |   |  |  |

|  |                 |  |  |
|--|-----------------|--|--|
| subjects affected / exposed                          | 2 / 24 (8.33%)  |  |  |
| occurrences (all)                                    | 2               |  |  |
| General disorders and administration site conditions |                 |  |  |
| Mucosal dryness                                      |                 |  |  |
| subjects affected / exposed                          | 7 / 24 (29.17%) |  |  |
| occurrences (all)                                    | 7               |  |  |

## **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