



Clinical trial results:

Dexmedetomidine pharmacokinetics-pharmacodynamics in mechanically ventilated neonates with single-organ respiratory failure (NEODEX)

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2010-023155-28 |
| Trial protocol | BE |
| Global end of trial date | 22 September 2016 |

Results information

| | |
|-----------------------------------|----------------------------|
| Result version number | v1 (current) |
| This version publication date | 08 September 2024 |
| First version publication date | 08 September 2024 |
| Summary attachment (see zip file) | Article (Neodex_paper.pdf) |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | AGO/2010/006 |
|-----------------------|--------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Ghent University Hospital |
| Sponsor organisation address | Corneel Heymanslaan 10, Ghent, Belgium, 9000 |
| Public contact | Hiruz CTU, Ghent University Hospital, 32 93320500, hiruz.ctu@uzgent.be |
| Scientific contact | Hiruz CTU, Ghent University Hospital, 32 93320500, hiruz.ctu@uzgent.be |

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 | 29 December 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 20 April 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 22 September 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

- what are the pharmacokinetic parameters (distribution volume, distribution half-life, terminal half-life, context-sensitive half-life, clearance) of dexmedetomidine infusion in mechanically ventilated neonates with single-organ respiratory failure?
- do size, age (postmenstrual, postconceptional, postnatal), co-medication, severity of illness, infusion length (covariates) contribute to a variability in exposure and response to dexmedetomidine in this population?
- knowledge of the pharmacokinetic parameters of dexmedetomidine and their covariates will allow targeted dosing in this population

Protection of trial subjects:

Ethics review and approval, informed consent, supportive care and routine monitoring.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 02 August 2011 |
| 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 | Belgium: 6 |
| Worldwide total number of subjects | 6 |
| EEA total number of subjects | 6 |

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) | 6 |
| From 65 to 84 years | 0 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

52 patients were screened in the period from 02-08-2011 till 17-09-2016. 35 patients were included, 34 patients were included and completed the trial. End of trial notification was dated 20-04-2017 (last patient last visit) and submitted to EC and CA 19-04-2017.

Only an evaluation of the 6 patients included in the pilot trial has been done.

Pre-assignment

Screening details:

Inclusion Criteria:

patient age less than 1 month (Male/Female) (step-down strategy for age)

first included patients (n=30): postmenstrual age \geq 34 weeks (near-term neonates)

following included patients (n=30) : postmenstrual age \geq 25 weeks and $<$ 34 weeks (preterm neonates)

patients with single-organ respiratory failure in need for analgo

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

| | |
|------------------------------|--------------|
| Are arms mutually exclusive? | No |
| Arm title | Baseline arm |

Arm description: -

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

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

Arm description: -

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | dexmedetomidine |
| Investigational medicinal product code | CAS 113775476 |
| Other name | Precedex 100µg/ml |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Dexmedetomidine 2 ml ampoule containing 200 mcg (100 mcg/ml) dexmedetomidine for dilution with 0,9 % sodium chloride injection.

| Number of subjects in period 1 | Baseline arm | Treatment arm |
|--------------------------------|--------------|---------------|
| Started | 6 | 6 |
| Completed | 6 | 6 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Baseline arm |
| Reporting group description: - | |
| Reporting group title | Treatment arm |
| Reporting group description: - | |

| Reporting group values | Baseline arm | Treatment arm | Total |
|---|--------------|---------------|-------|
| Number of subjects | 6 | 6 | 6 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous | | | |
| Postmenstrual age | | | |
| Units: weeks | | | |
| arithmetic mean | 39 | 39 | |
| full range (min-max) | 34 to 44 | 34 to 44 | - |
| Gender categorical Units: Subjects | | | |
| Female | 3 | 3 | 3 |
| Male | 3 | 3 | 3 |
| Reason for admission Units: Subjects | | | |
| respiratory distress syndrome | 3 | 3 | 3 |
| hernia diaphragmatica | 1 | 1 | 1 |
| oesophageal atresia repair | 1 | 1 | 1 |
| respiratory syncytial virus | 1 | 1 | 1 |
| Weight Units: kg | | | |
| arithmetic mean | 3.18 | 3.18 | |
| full range (min-max) | 2.25 to 4.1 | 2.25 to 4.1 | - |

End points

End points reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Baseline arm |
| Reporting group description: - | |
| Reporting group title | Treatment arm |
| Reporting group description: - | |

Primary: Standardised population clearance

| | |
|------------------------|-----------------------------------|
| End point title | Standardised population clearance |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Overall trial | |

| End point values | Baseline arm | Treatment arm | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6 | 6 | | |
| Units: L/h | | | | |
| number (not applicable) | 42.1 | 42.1 | | |

Statistical analyses

| | |
|---|-----------------------------------|
| Statistical analysis title | standardised population clearance |
| Statistical analysis description: | |
| See article in attachment | |
| Comparison groups | Baseline arm v Treatment arm |
| Number of subjects included in analysis | 12 |
| Analysis specification | Post-hoc |
| Analysis type | other ^[1] |
| P-value | = 0 ^[2] |
| Method | see attachment |
| Confidence interval | |
| level | 95 % |

Notes:

[1] - See article in attachment

[2] - See article in attachment

Secondary: standardised population central volume

| | |
|------------------------|---|
| End point title | standardised population central volume ^[3] |
| End point description: | |

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Overall study | |
| Notes: | |
| [3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. | |
| Justification: See article in attachment | |

| End point values | Treatment arm | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: Liter | | | | |
| number (not applicable) | 80.4 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: standardised population inter-compartmental clearance

| | |
|------------------------|--|
| End point title | standardised population inter-compartmental clearance ^[4] |
| End point description: | |

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Overall study | |
| Notes: | |
| [4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. | |
| Justification: See article in attachment | |

| End point values | Treatment arm | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: L/h | | | | |
| number (not applicable) | 12.5 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: standardised population peripheral volume

| | |
|------------------------|--|
| End point title | standardised population peripheral volume ^[5] |
| End point description: | |

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Overall trial | |

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: See article in attachment

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | Treatment arm | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: Liter | | | | |
| number (not applicable) | 142 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: maturation half-life

| | |
|-----------------|-------------------------------------|
| End point title | maturation half-life ^[6] |
|-----------------|-------------------------------------|

End point description:

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

End point timeframe:

Overall trial

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: See article in attachment

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | Treatment arm | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: week | | | | |
| number (not applicable) | 36.4 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall study

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Baseline arm |
|-----------------------|--------------|

Reporting group description: -

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

Reporting group description: -

| Serious adverse events | Baseline arm | Treatment arm | |
|---|---------------|---------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 6 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | Baseline arm | Treatment arm | |
|---|------------------------------|----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 6 (16.67%) | |
| Cardiac disorders | | | |
| Bradychardia | Additional description: mild | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 17 February 2012 | Amendment 5 Description of the substantial amendment: After analysis of the blood concentrations of dexmedetomidin, there was no lower clearing identified, compared to the non-cardiosurgical subpopulation (n = 18). Therefore, the investigators wish to keep the identical dosing regime for the non-surgical patient population. Secondly, they wish to have the possibility to increase the infusion rate of the study medication once, to lean closer to the clinical practice of analgosedation. This because retrospective analysis of the research population showed a need of rescue medication (fentanyl) in > 50 % of the study patients. |
| 10 February 2015 | Amendment 9 Reasons for the substantial amendment: Admission of patients after cardiac surgery. |
| 25 August 2015 | Amendment 10 Reason for the substantial amendment: change of dosing regime |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/31312867>