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 Hostital, 32 93320500, hiruz.ctu@uzgent.be
Scientific contact	Hiruz CTU, Ghent University Hostital, 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 >= 34 weeks (near-term neonates)
following included patients (n=30) : postmenstrual age >= 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 full range (min-max)	 39 34 to 44	 39 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