



## Clinical trial results:

## Bioavailability and pharmacokinetics of intranasal dexmedetomidine in children

### Summary

EudraCT number	2016-002880-33
Trial protocol	FI
Global end of trial date	10 September 2018

### Results information

Result version number	v1 (current)
This version publication date	25 October 2020
First version publication date	25 October 2020
Summary attachment (see zip file)	PINDEX_article (47_Uusalo_PINDEX_Anesth_Analg_article.pdf)

### Trial information

#### Trial identification

Sponsor protocol code	PINDEX
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#### Additional study identifiers

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

Notes:

### Sponsors

Sponsor organisation name	University of Turku
Sponsor organisation address	Kiinamyllynkatu 4-8, Turku, Finland,
Public contact	Turku Clinical Research Centre, Turku University Hospital, turkucrc@tyks.fi
Scientific contact	Turku Clinical Research Centre, Turku University Hospital, turkucrc@tyks.fi

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	10 September 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2017
Global end of trial reached?	Yes
Global end of trial date	10 September 2018
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:

We aim to characterize the pharmacokinetics of dexmedetomidine after intranasal dosing.

Protection of trial subjects:

Normal hospital routines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2016
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	Finland: 55
Worldwide total number of subjects	55
EEA total number of subjects	55

Notes:

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**Subjects enrolled per age group**

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In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	8
Children (2-11 years)	47
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Patients (and their guardians) potentially eligible for the study were approached for information, assessment of eligibility criteria, and consent either during a preceding clinic visit or on arrival in the hospital for the procedure.

### Pre-assignment

Screening details:

Patients potentially eligible (155) for the study were approached for information, assessment of eligibility criteria, and consent either during a preceding clinic visit or on arrival in the hospital for the procedure. Written informed consent was obtained from 55 patients.

### Pre-assignment period milestones

Number of subjects started	55
Intermediate milestone: Number of subjects	Informed consent: 55
Number of subjects completed	55

### Period 1

Period 1 title	Study clinical phase (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Arm title	IN dexmedetomidine
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	dexmedetomidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, solution in single-dose container
Routes of administration	Intranasal use

Dosage and administration details:

A dose of 2–3 µg·kg<sup>-1</sup> of dexmedetomidine (dexmedetomidine hydrochloride 118 µg·milliliter<sup>-1</sup>, corresponding to dexmedetomidine base 100 µg·milliliter<sup>-1</sup>, Dexdor; Orion Pharma, Espoo, Finland) was administered IN using an LMA® MAD Nasal™ device (Teleflex MAD Nasal; Teleflex Inc, Research Triangle Park, NC) approximately 45–60 minutes before the scheduled MRI procedure

<b>Number of subjects in period 1</b>	IN dexmedetomidine
Started	55
Clinical phase ended	55
Completed	50
Not completed	5
Protocol deviation	5



## Baseline characteristics

### Reporting groups

Reporting group title	Study clinical phase
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Reporting group description: -

Reporting group values	Study clinical phase	Total	
Number of subjects	55	55	
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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
median	5.0		
standard deviation	± 2.4	-	
Gender categorical			
Units: Subjects			
Female	27	27	
Male	28	28	
Ethnic group			
Units: Subjects			
Caucasian	55	55	

### Subject analysis sets

Subject analysis set title	Final analysis
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Our primary outcome was to determine the peak plasma concentrations (C<sub>max</sub>) and time to C<sub>max</sub> (t<sub>max</sub>) after IN dexmedetomidine. We hypothesized that IN 2–3 µg·kg<sup>-1</sup> dexmedetomidine leads to previously defined clinically effective plasma concentrations and coincide with the onset of action during MRI sedation in pediatric patients. Our secondary outcomes were area under time–concentration curve from 0 to 4 hours (AUC<sub>0–4h</sub>) and the pharmacological effects caused by single IN dexmedetomidine to pharmacokinetics during pediatric sedation. We also evaluated the effect of age on dexmedetomidine pharmacokinetics and the effect our dosing regimen had on inducing clinically significant sedative effects in this patient population.

Reporting group values	Final analysis		
Number of subjects	1		
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 Units: years median standard deviation	5.0 ± 2.4		
Gender categorical Units: Subjects			
Female Male	25 25		
Ethnic group Units: Subjects			
Caucasian	50		

## End points

### End points reporting groups

Reporting group title	IN dexmedetomidine
Reporting group description:	-
Subject analysis set title	Final analysis
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Our primary outcome was to determine the peak plasma concentrations (C<sub>max</sub>) and time to C<sub>max</sub> (t<sub>max</sub>) after IN dexmedetomidine. We hypothesized that IN 2–3 µg·kg<sup>-1</sup> dexmedetomidine leads to previously defined clinically effective plasma concentrations and coincide with the onset of action during MRI sedation in pediatric patients. Our secondary outcomes were area under time–concentration curve from 0 to 4 hours (AUC<sub>0–4h</sub>) and the pharmacological effects caused by single IN dexmedetomidine to pharmacokinetics during pediatric sedation. We also evaluated the effect of age on dexmedetomidine pharmacokinetics and the effect our dosing regimen had on inducing clinically significant sedative effects in this patient population.

### Primary: Peak plasma concentration

End point title	Peak plasma concentration
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End point description:

End point type	Primary
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End point timeframe:

0–4 hours

End point values	IN dexmedetomidine	Final analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	50	50		
Units: nanogram(s)/milliliter				
arithmetic mean (standard deviation)	0.0011 (± 0.0051)	0.0011 (± 0.0051)		

### Statistical analyses

Statistical analysis title	Final analysis
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Statistical analysis description:

descriptive analysis

Comparison groups	IN dexmedetomidine v Final analysis
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Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other <sup>[1]</sup>
P-value	< 0.05
Method	ANOVA

Notes:

[1] - descriptive analysis



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

During administration of IN dexmedetomidine and thereafter at 1, 2, 3, and 4 hours after dosing

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	10
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### Reporting groups

Reporting group title	IN dexmedetomidine
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Reporting group description: -

Reporting group title	All patients
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Reporting group description: -

Serious adverse events	IN dexmedetomidine	All patients	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 55 (0.00%)	0 / 55 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	IN dexmedetomidine	All patients	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 55 (1.82%)	1 / 55 (1.82%)	
Cardiac disorders			
Bradycardia	Additional description: One patient (5 years, 17 kg) received a single dose of atropine for bradycardia of 36 minute-1, occurring soon after dosing of thiopental, 57 minutes after dexmedetomidine		
subjects affected / exposed	1 / 55 (1.82%)	1 / 55 (1.82%)	
occurrences (all)	1	1	

## 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

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/31206433>