



## Clinical trial results:

### Pharmacokinetics of intravenous, rectal, intravesical, vaginal, and transdermal administration of exogenous melatonin in healthy female volunteers: a crossover study

#### Summary

EudraCT number	2017-000997-13
Trial protocol	DK
Global end of trial date	01 February 2021

#### Results information

Result version number	v1 (current)
This version publication date	17 February 2021
First version publication date	17 February 2021
Summary attachment (see zip file)	Summary attachment (Report.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	HEHDZ01
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03519750
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	Center for Perioperative Optimization, Department of Surgery
Sponsor organisation address	Borgmester Ib Juuls Vej 1, Herlev, Denmark, 2730
Public contact	Dennis Zetner, Center for Perioperative Optimization, Gastroenheden D, Herlev Hospital, dennis.zetner@gmail.com
Scientific contact	Dennis Zetner, Center for Perioperative Optimization, Gastroenheden D, Herlev Hospital, dennis.zetner@gmail.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**

Analysis stage	Final
Date of interim/final analysis	18 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 May 2020
Global end of trial reached?	Yes
Global end of trial date	01 February 2021
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

Main objective of the trial:

The aim of the study is to determine the pharmacokinetic properties, and possible adverse reactions of melatonin when administered rectally, intravesically, vaginally, transdermally and intravenously, in healthy female volunteers.

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

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**Population of trial subjects****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)	10
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Participants were recruited by an ad for medical students of the University of Copenhagen. All 10 participants were recruited in November/December 2018.

### Pre-assignment

Screening details:

After contacting the primary investigator, possible participants showed up at the hospital. All participants were screened for eligibility criteria. All 10 volunteers were deemed eligible by the primary investigator.

### Pre-assignment period milestones

Number of subjects started	10
Number of subjects completed	10

### Period 1

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

### Arms

Arm title	Arm 1
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Arm description:

Intravenous administration

Arm type	Experimental
Investigational medicinal product name	Intravenous Melatonin
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

25 mg

Investigational medicinal product name	Intravesical Melatonin
Investigational medicinal product code	PR2
Other name	
Pharmaceutical forms	Intravesical suspension
Routes of administration	Intravesical use

Dosage and administration details:

25 mg

Investigational medicinal product name	Vaginal Melatonin
Investigational medicinal product code	PR3
Other name	
Pharmaceutical forms	Vaginal capsule, soft
Routes of administration	Vaginal use

Dosage and administration details:

25 mg

Investigational medicinal product name	Rectal melatonin
Investigational medicinal product code	PR4
Other name	
Pharmaceutical forms	Rectal emulsion
Routes of administration	Rectal use
Dosage and administration details:	
25 mg	
Investigational medicinal product name	Transdermal melatonin
Investigational medicinal product code	PR5
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use
Dosage and administration details:	
25 mg/g, 1 g applied	

<b>Number of subjects in period 1</b>	Arm 1
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	
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	23		
full range (min-max)	22 to 27	-	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	0	0	
Ethnicity			
Units: Subjects			
Caucasian	9	9	
Asian	1	1	
Height			
Units: cm			
median	172		
full range (min-max)	163 to 184	-	
Weight			
Units: kg			
median	64		
full range (min-max)	54 to 71	-	
BMI			
Units: kg/m2			
median	21.1		
full range (min-max)	18.7 to 23.1	-	

## End points

### End points reporting groups

Reporting group title	Arm 1
Reporting group description: Intravenous administration	

### Primary: Pharmacokinetic Properties

End point title	Pharmacokinetic Properties <sup>[1]</sup>
End point description:	

End point type	Primary
End point timeframe: Over 48 hours.	

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: No statistical tests have been performed, only pharmacokinetic calculations. I am unable to enter these, as I have not calculated any p-values.

End point values	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: variable				
number (not applicable)	10			

<b>Attachments (see zip file)</b>	Table 3.docx
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### Statistical analyses

No statistical analyses for this end point

### Secondary: SRT and KSS

End point title	SRT and KSS
End point description:	

End point type	Secondary
End point timeframe: 48 hours	

<b>End point values</b>	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: variable				
number (not applicable)	10			

<b>Attachments (see zip file)</b>	Table 4.docx
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### Statistical analyses

No statistical analyses for this end point

### Secondary: Adverse reactions

End point title	Adverse reactions
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End point description:

End point type	Secondary
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End point timeframe:

24-48 hours after administration.

<b>End point values</b>	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: n	10			

<b>Attachments (see zip file)</b>	Table 5.docx
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### Statistical analyses

No statistical analyses for this end point

## Adverse events

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

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Timeframe for reporting adverse events:

24-48 hours after administration of melatonin

Assessment type	Non-systematic
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### Dictionary used

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Dictionary name	MedDRA
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Dictionary version	23
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Frequency threshold for reporting non-serious adverse events: 0 %

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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: These are reported under secondary outcomes.



## 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/32937627>