



## Clinical trial results:

### Double blind randomised controlled trial of exogenous administration of melatonin in chronic pain (DREAM-CP)

#### Summary

EudraCT number	2018-004048-50
Trial protocol	GB
Global end of trial date	11 September 2022

#### Results information

Result version number	v1 (current)
This version publication date	25 January 2025
First version publication date	25 January 2025
Summary attachment (see zip file)	DREAM-CP data summary (DREAM-CP results summary.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	3-062-18
-----------------------	----------

##### Additional study identifiers

ISRCTN number	ISRCTN12861060
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	University of Aberdeen
Sponsor organisation address	Foresterhil, Aberdeen, United Kingdom, AB252ZD
Public contact	Professor /Co-investigator, University of Aberdeen, +44 07900603649, h.f.galley@abdn.ac.uk
Scientific contact	Professor /Co-investigator, University of Aberdeen, +44 07900603649, h.f.galley@abdn.ac.uk

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	08 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 March 2022
Global end of trial reached?	Yes
Global end of trial date	11 September 2022
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Does melatonin treatment improve sleep disturbance in patients with chronic pain?

Protection of trial subjects:

All staff working on the trial are GCP trained and have a thorough understanding of anticipated adverse events and the reporting process of these events.

The sponsor is notified of any serious adverse event within 24 hours as per protocol.

The Data Monitoring Committee (DMC) are assigned to review overall safety data to identify safety issues which may not be apparent on an individual case basis.

Background therapy:

Melatonin will be administered as Circadin (2mg tablets, Flynn Pharmaceuticals Ltd.) which has EMA regulatory approval and is a slow release formulation with a blood concentration profile resembling that of endogenous melatonin

Evidence for comparator: -

Actual start date of recruitment	01 February 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 60
Worldwide total number of subjects	60
EEA total number of subjects	0

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)	46
From 65 to 84 years	14

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

## Subject disposition

### Recruitment

Recruitment details:

Participants are recruited from the Pain clinical Aberdeen Royal Infirmary

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

Number of subjects started	60
Number of subjects completed	60

### Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Group A

Arm description:

Received Melatonin first then placebo after washout period

Arm type	melatonin first
Investigational medicinal product name	2mg oral Circadin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2mg Circadin taken 2 hours before planned bedtime

<b>Arm title</b>	Group B
------------------	---------

Arm description:

Received Placebo first then melatonin after washout period

Arm type	receive placebo before active drug
Investigational medicinal product name	2mg oral placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2mg placebo taken 2 hours before planned bedtime

Number of subjects in period 1	Group A	Group B
Started	30	30
Completed	30	28
Not completed	0	2
Consent withdrawn by subject	-	2

## Period 2

Period 2 title	Period 1
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Group A

Arm description:

Received Melatonin first then placebo after washout period

Arm type	melatonin first
Investigational medicinal product name	2mg oral Circadin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2mg Circadin taken 2 hours before planned bedtime

<b>Arm title</b>	Group B
------------------	---------

Arm description:

Received Placebo first then melatonin after washout period

Arm type	receive placebo before active drug
Investigational medicinal product name	2mg oral placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2mg placebo taken 2 hours before planned bedtime

Number of subjects in period 2	Group A	Group B
Started	30	28
Completed	27	27
Not completed	3	1
Consent withdrawn by subject	3	1

### Period 3

Period 3 title	Washout period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

DREAM-CP is a crossover randomised trial. The washout out period is the crossover period.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Group A

Arm description:

Received Melatonin first then placebo after washout period

Arm type	melatonin first
Investigational medicinal product name	2mg oral Circadin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2mg Circadin taken 2 hours before planned bedtime

<b>Arm title</b>	Group B
------------------	---------

Arm description:

Received Placebo first then melatonin after washout period

Arm type	receive placebo before active drug
Investigational medicinal product name	2mg oral placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2mg placebo taken 2 hours before planned bedtime

Number of subjects in period 3	Group A	Group B
Started	27	27
Completed	26	25
Not completed	1	2
Consent withdrawn by subject	1	2

#### Period 4

Period 4 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

#### Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

<b>Arm title</b>	Group A
------------------	---------

Arm description:

Received Melatonin first then placebo after washout period

Arm type	melatonin first
Investigational medicinal product name	2mg oral Circadin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2mg Circadin taken 2 hours before planned bedtime

<b>Arm title</b>	Group B
------------------	---------

Arm description:

Received Placebo first then melatonin after washout period

Arm type	receive placebo before active drug
Investigational medicinal product name	2mg oral placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2mg placebo taken 2 hours before planned bedtime

<b>Number of subjects in period 4</b>	Group A	Group B
Started	26	25
Completed	26	25



## Baseline characteristics

### Reporting groups

Reporting group title	Group A
Reporting group description:	
Received Melatonin first then placebo after washout period	
Reporting group title	Group B
Reporting group description:	
Received Placebo first then melatonin after washout period	

Reporting group values	Group A	Group B	Total
Number of subjects	30	30	60
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	19	27	46
From 65-84 years	11	3	14
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	57.9	54.61	
standard deviation	± 14.03	± 11.92	-
Gender categorical			
Units: Subjects			
Female	20	16	36
Male	10	14	24

### Subject analysis sets

Subject analysis set title	DREAM Per Protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
DREAM Per protocol	
Subject analysis set title	DREAM Intention-to-treat
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
DREAM intention to treat	

Reporting group values	DREAM Per Protocol	DREAM Intention-to-treat	
Number of subjects	51	58	

Age categorical			
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)	42	44	
From 65-84 years	9	14	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	
Gender categorical			
Units: Subjects			
Female	33	36	
Male	18	22	

## End points

### End points reporting groups

Reporting group title	Group A
Reporting group description: Received Melatonin first then placebo after washout period	
Reporting group title	Group B
Reporting group description: Received Placebo first then melatonin after washout period	
Reporting group title	Group A
Reporting group description: Received Melatonin first then placebo after washout period	
Reporting group title	Group B
Reporting group description: Received Placebo first then melatonin after washout period	
Reporting group title	Group A
Reporting group description: Received Melatonin first then placebo after washout period	
Reporting group title	Group B
Reporting group description: Received Placebo first then melatonin after washout period	
Reporting group title	Group A
Reporting group description: Received Melatonin first then placebo after washout period	
Reporting group title	Group B
Reporting group description: Received Placebo first then melatonin after washout period	
Reporting group title	Group A
Reporting group description: Received Melatonin first then placebo after washout period	
Reporting group title	Group B
Reporting group description: Received Placebo first then melatonin after washout period	
Subject analysis set title	DREAM Per Protocol
Subject analysis set type	Per protocol
Subject analysis set description: DREAM Per protocol	
Subject analysis set title	DREAM Intention-to-treat
Subject analysis set type	Intention-to-treat
Subject analysis set description: DREAM intention to treat	

### Primary: Primary outcome

End point title	Primary outcome
End point description:	
End point type	Primary
End point timeframe: The primary outcome measure was VSH sleep disturbance after 6 weeks of treatment.	

<b>End point values</b>	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	28		
Units: none				
median (full range (min-max))	481 (67 to 632)	409 (122 to 673)		

## Statistical analyses

<b>Statistical analysis title</b>	linear mixed model
Comparison groups	Group A v Group B
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Mixed models analysis

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

24 Hours

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

### Dictionary used

Dictionary name	No dictionary used
-----------------	--------------------

Dictionary version	n/a
--------------------	-----

### Reporting groups

Reporting group title	Group A
-----------------------	---------

Reporting group description:

Received Melatonin first then placebo after washout period

Reporting group title	Group B
-----------------------	---------

Reporting group description:

Received Placebo first then melatonin after washout period

Serious adverse events	Group A	Group B	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	2 / 28 (7.14%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Lower respiratory tract infection			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Appendicitis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	Group A	Group B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 30 (76.67%)	16 / 28 (57.14%)	
General disorders and administration site conditions			
General physical condition abnormal			
subjects affected / exposed	23 / 30 (76.67%)	16 / 28 (57.14%)	
occurrences (all)	23	16	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

---

### 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/38355388>