



## Clinical trial results: Phase shift in adult ADHD of sleep and appetite.

### Summary

EudraCT number	2012-000320-18
Trial protocol	NL
Global end of trial date	02 July 2019

### Results information

Result version number	v1 (current)
This version publication date	29 July 2021
First version publication date	29 July 2021

### Trial information

#### Trial identification

Sponsor protocol code	FASE01
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Dutch Trail Register: #NTR3831

Notes:

#### Sponsors

Sponsor organisation name	Parnassia Bavo Groep
Sponsor organisation address	Denemarkenlaan 2, Zoetermeer, Netherlands, 2711 EL
Public contact	Dr. D. Bijlenga, PsyQ Haaglanden, +31 0883573076, d.bijlenga@psyq.nl
Scientific contact	Dr. D. Bijlenga, PsyQ Haaglanden, +31 0883573076, d.bijlenga@psyq.nl

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	06 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 July 2019
Global end of trial reached?	Yes
Global end of trial date	02 July 2019
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

Main objective of the trial:

To investigate the best treatment of the Delayed Sleep Phase Syndrome in adults with ADHD.

Protection of trial subjects:

In case that disadvantages participation in the current trial outweigh the advantages, the ethical committee will be informed. The study will be suspended pending further review by the reviewing ethical committee, unless this suspension could harm the health of the participants.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects****Subjects enrolled per country**

Country: Number of subjects enrolled	Netherlands: 51
Worldwide total number of subjects	51
EEA total number of subjects	51

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)	51
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Participants were recruited from June 2013 to August 2016 and from April 2018 to June 2019 and followed up for 7 weeks after baseline. Participants were recruited from a outpatient clinic of PsyQ Adult ADHD.

### Pre-assignment

Screening details:

Inclusion: age between 18 and 55 y; fluency in the Dutch language; clinical diagnosis of both ADHD and DSPS. Exclusion: severe psychiatric disorders that need immediate treatment, neurological disorders, neurodegenerative diseases, mental retardation, shiftwork or BLT within the last month, pregnancy.

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

Participants were randomly assigned, following simple randomization procedures (computer-generated randomization numbers)

### Arms

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

Arm description:

0.5 mg/d melatonin

Arm type	Experimental
Investigational medicinal product name	Melatonin
Investigational medicinal product code	73-31-4
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1mg per day

<b>Arm title</b>	Placebo
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Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet a day

<b>Arm title</b>	Melatonin + BLT
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Arm description:

Melatonin + Bright Light Therapy

Arm type	Experimental
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Investigational medicinal product name	Melatonin
Investigational medicinal product code	73-31-4
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

0.5 mg per day

<b>Number of subjects in period 1<sup>[1]</sup></b>	Melatonin	Placebo	Melatonin + BLT
Started	17	17	15
Completed	17	14	15
Not completed	0	3	0
Lost to follow-up	-	3	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Two participants dropped out prior to the baseline measurement because they were not willing or able to fulfill the study demands

## Baseline characteristics

### Reporting groups

Reporting group title	Melatonin
Reporting group description: 0.5 mg/d melatonin	
Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	Melatonin + BLT
Reporting group description: Melatonin + Bright Light Therapy	

Reporting group values	Melatonin	Placebo	Melatonin + BLT
Number of subjects	17	17	15
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			
Age			
Units: years			
arithmetic mean	28.82	30.06	29.73
standard deviation	± 7.91	± 6.89	± 11.42
Gender categorical			
gender			
Units: Subjects			
Female	10	11	11
Male	7	6	4

Reporting group values	Total		
Number of subjects	49		
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			
Age			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
gender			
Units: Subjects			
Female	32		
Male	17		

## End points

### End points reporting groups

Reporting group title	Melatonin
Reporting group description: 0.5 mg/d melatonin	
Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	Melatonin + BLT
Reporting group description: Melatonin + Bright Light Therapy	

### Primary: DLMO

End point title	DLMO
End point description:	
End point type	Primary
End point timeframe: The primary outcome, DLMO, was assessed at baseline (T0), the day after the 3-week treatment period (T1), and 2 weeks after the end of treatment (T2).	

End point values	Melatonin	Placebo	Melatonin + BLT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	17	15	
Units: time				
arithmetic mean (standard deviation)	2239 (± 225)	2257 (± 219)	2311 (± 139)	

### Statistical analyses

Statistical analysis title	Main effects
Statistical analysis description: The effects of the three interventions on DLMO and ADHD-RS scores were compared using linear mixed models with T0 as reference, and corrected for baseline values of the outcomes.	
Comparison groups	Placebo v Melatonin v Melatonin + BLT
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis

Confidence interval	
level	95 %
sides	2-sided

## Secondary: ADHD symptoms

End point title	ADHD symptoms
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End point description:

End point type	Secondary
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End point timeframe:

The secondary outcome, ADHD symptoms, were assessed at baseline (T0), the day after the 3-week treatment period (T1), and 2 weeks after the end of treatment (T2).

End point values	Melatonin	Placebo	Melatonin + BLT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	17	15	
Units: points				
arithmetic mean (standard deviation)	32.35 (± 6.60)	33.40 (± 9.13)	34.13 (± 5.13)	

## 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:  
within 15 days after the event happened.

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Assessment type	Non-systematic
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### Dictionary used

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Dictionary name	ToetsingOnline
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Dictionary version	x
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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: No non-serious adverse events happened over the course of the study.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 February 2014	Venapuncture or finger prick is added as alternative to a venflon for the blood sampling.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
01 August 2016	due to a change in junior researchers, we were required to pause the inclusion of the study.	02 April 2018

Notes:

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/33121289>