Clinical trial results:
The effect of agomelatine on CLOCK gene expression in patients with major depressive disorder and healthy controls: an exploratory study.

Summary

EudraCT number	2010-021044-17
Trial protocol	AT
Global end of trial date	04 November 2011

Results information

Result version number	v1 (current)
This version publication date	21 September 2019
First version publication date	21 September 2019

Trial information

Trial identification

Sponsor protocol code	CLOCK_depression

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Spitalgasse 23, Vienna, Austria, 1090
Public contact	Department of Clinical Pharmacology, Department of Clinical Pharmacology, 0043 14040029810,
Scientific contact	Department of Clinical Pharmacology, Department of Clinical Pharmacology, 0043 14040029810,

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	05 December 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 November 2011
Global end of trial reached?	Yes
Global end of trial date	04 November 2011
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Rhythmic 24hour mRNA expression of CLOCK genes,
differences in transcript levels of CLOCK genes,
differences in the genome-wide gene expression,
assessed in mRNA from peripheral blood leucocytes.

Protection of trial subjects:

Subjects were during the trial under the supervision of a physician or an experienced nurse.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 September 2010
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	Austria: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	9
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited by use of the data base of the Dep. of Clinical Pharmacology, Medical University of Vienna.

Pre-assignment

Screening details:

Check of the in- and exclusion criteria, physical examination, vital signs, laboratory assessment and ECG recording

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?	Yes
Arm title	Study group A healthy subjects

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Agomelatine (VALDOXAN 25 mg – Filmtabletten)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Intake of VALDOXAN 25 mg coated tablets, once a day at 11:00 PM ± 1 hour for 14 consecutive days. is foreseen

Arm title	Study group B Patients with MDD

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Agomelatine (VALDOXAN 25 mg – Filmtabletten)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Intake of VALDOXAN 25 mg coated tablets, once a day at 11:00 PM ± 1 hour for 14 consecutive days. is foreseen

Number of subjects in period 1	Study group A healthy subjects	Study group B Patients with MDD
Started	5	4
Completed	4	4
Not completed	1	0
Physician decision	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	9	9	
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)	9	9	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	6	6	
Male	3	3	

End points

End points reporting groups

Reporting group title	Study group A healthy subjects
Reporting group description: -	
Reporting group title	Study group B Patients with MDD
Reporting group description: -	

Primary: Differences in leucocyte CLOCK gene expression in depressed patients before and after agomelatine treatment

End point title	Differences in leucocyte CLOCK gene expression in depressed patients before and after agomelatine treatment
End point description:	

End point type	Primary
End point timeframe:	
14 days	

End point values	Study group A healthy subjects	Study group B Patients with MDD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: other	4	4		

Statistical analyses

Statistical analysis title	Statistics to end point
Comparison groups	Study group B Patients with MDD v Study group A healthy subjects
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0001
Method	Wilcoxon (Mann-Whitney)

Primary: Differences in leucocyte CLOCK gene expression in healthy subjects before and after agomelatine treatment

End point title	Differences in leucocyte CLOCK gene expression in healthy subjects before and after agomelatine treatment
End point description:	

End point type	Primary
End point timeframe: 14 days	

End point values	Study group A healthy subjects	Study group B Patients with MDD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: other	4	4		

Statistical analyses

Statistical analysis title	Statistics to end point
Comparison groups	Study group A healthy subjects v Study group B Patients with MDD
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0001
Method	Wilcoxon (Mann-Whitney)

Primary: Comparision between lecocyte CLOCK gene expression between healthy subjects and patients at baseline and after agomelatine treatment

End point title	Comparision between lecocyte CLOCK gene expression between healthy subjects and patients at baseline and after agomelatine treatment
End point description:	

End point type	Primary
End point timeframe: 14 days	

End point values	Study group A healthy subjects	Study group B Patients with MDD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: other	4	4		

Statistical analyses

Statistical analysis title	End point statistic
Comparison groups	Study group A healthy subjects v Study group B Patients with MDD
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0001
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 20.10.2010-04.11.2011	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	Adverse events overall trial

Reporting group description: -

Serious adverse events	Adverse events overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Adverse events overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 9 (77.78%)		
Vascular disorders			
Angina			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Migraine			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
General disorders and administration site conditions			

Malaise subjects affected / exposed occurrences (all) Fatigue during exercise subjects affected / exposed occurrences (all) Tiredness subjects affected / exposed occurrences (all) Pain (lower abdomen) subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 2 1 / 9 (11.11%) 5 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1		
Reproductive system and breast disorders Menstrual disorder subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Gastrointestinal disorders sore throat subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Psychiatric disorders Dysphoria subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		

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? Yes

Date	Interruption	Restart date
04 November 2011	Unsuccessful recruitment	-

Notes:

Limitations and caveats

None reported