Clinical trial results:
Randomized double-blind, placebo controlled study with NEURAPAS® balance in addition to psychoeducation or psychotherapy in adolescents from 12 to 17 years suffering from mild depressive episodes with nervous restlessness

Summary

EudraCT number	2012-004627-20
Trial protocol	DE
Global end of trial date	10 February 2014

Results information

Result version number	v1
This version publication date	04 July 2016
First version publication date	23 July 2015

Trial information

Trial identification

Sponsor protocol code	176S11NB

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	PASCOE pharmazeutische Präparate GmbH
Sponsor organisation address	Schiffenberger Weg 55, Giessen, Germany, 35394
Public contact	Project manager, PASCOE pharmazeutische Präparate GmbH, 0049 641-7960-963, bianka.krick@gmx.de
Scientific contact	Project manager, PASCOE pharmazeutische Präparate GmbH, 0049 641-7960-963, bianka.krick@gmx.de

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	27 May 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 February 2014
Global end of trial reached?	Yes
Global end of trial date	10 February 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective was to prove superiority of NEURAPAS® balance (pooled data of both dosages) compared to placebo in improving depressive symptoms, measured by means of the German version of the CDRS-R (Children's Depression Rating Scale, Revised) after 6 weeks treatment

Protection of trial subjects:

The only measure in this trial with a potential risk for the participants was blood sampling, where e.g. pain, bruises, hematoma, injury of nerves or infections may occur. No adverse events due to the blood sampling occured. Further risks due to the trial design or trial measures were not expected.

Study was terminated on 10th Feb 2014 due to insufficient patient recruitment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 April 2013
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	Germany: 4
Worldwide total number of subjects	4
EEA total number of subjects	4

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)	4
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Germany: July 13 - Feb 14: 5 pat were enrolled: 1 pat was screening failure, 4 pat were randomized (1x verum 3x1, 2x verum 3x2 and 1x placebo): 2 of these pat were drop outs (due to "pat's wish" and "pat developed suicidal ideations").

Pre-assignment

Screening details:

Germany: July 13 - Feb 14: 5 pat were enrolled: 1 pat was screening failure, 4 pat were randomized: 2 of these pat were drop outs. Due to an error of the database, it is not possible to enter correct number of enrolled pat (acc. Email 30/04/15 'The system cannot differentiate between treated and enrolled.'). Complete data for 2 pat are assessable.

Period 1

Period 1 title	treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	3x2 verum

Arm description:

patient received 3x2 tbl a day verum

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

Dosage and administration details:

NEURAPAS® balance 3 x 2 film-coated tablets daily
Each film-coated tablet contains
- 60 mg dry extract from St John's Wort Herb (Hypericum perforatum L.), drug-extract ratio 4.6-6.5:1, extraction solvent ethanol 38 % m/m;
- 28 mg dry extract from Valerian Root (Valeriana officinalis L.), drug-extract ratio 3.8-5.6:1, extraction solvent ethanol 40 % m/m; and
- 32 mg dry extract) from Passion Flower Herb (Passiflora incarnata L.), drug-extract ratio 6.25-7.1:1, extraction solvent ethanol 60 % m/m.

Arm title	3x1 verum

Arm description:

patients received 3x1 tbl a day verum and 3x1 tbl a day placebo

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

Dosage and administration details:

NEURAPAS® balance 3 x 1 film-coated tablets daily + Placebo, 3 x 1 film-coated tablets daily

Verum contains:

- 60 mg dry extract from St John's Wort Herb (Hypericum perforatum L.), drug-extract ratio 4.6-6.5:1, extraction solvent ethanol 38 % m/m;
- 28 mg dry extract from Valerian Root (Valeriana officinalis L.), drug-extract ratio 3.8-5.6:1, extraction solvent ethanol 40 % m/m; and
- 32 mg dry extract) from Passion Flower Herb (Passiflora incarnata L.), drug-extract ratio 6.25-7.1:1, extraction solvent ethanol 60 % m/m.

Placebo contains:
None

Arm title	placebo

Arm description:

patients received 3x2 tbl a day 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:

Placebo, 3 x 2 film-coated tablets daily
Pharmacologic active ingredients: None
Other ingredients: Lactose 1H2O, talcum, magnesium stearate, alkaline butyl methacrylate copolymer (Eudragit E), macrogol 6000, titanium dioxide (E 171), indigocarmine (E 132).

Number of subjects in period 1	3x2 verum	3x1 verum	placebo
Started	2	1	1
Completed	0	1	1
Not completed	2	0	0
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	3x2 verum
Reporting group description:	
patient received 3x2 tbl a day verum	
Reporting group title	3x1 verum
Reporting group description:	
patients received 3x1 tbl a day verum and 3x1 tbl a day placebo	
Reporting group title	placebo
Reporting group description:	
patients received 3x2 tbl a day placebo	

Reporting group values	3x2 verum	3x1 verum	placebo
Number of subjects	2	1	1
Age categorical			
age of patients in years			
Units: Subjects			
Adolescents (12-17 years)	2	1	1
Age continuous			
age of patients in years (mean value)			
Units: years			
arithmetic mean	16	17	13
full range (min-max)	16 to 16	17 to 17	13 to 13
Gender categorical			
gender of the patients			
Units: Subjects			
Female	2	1	1
Male	0	0	0

Reporting group values	Total		
Number of subjects	4		
Age categorical			
age of patients in years			
Units: Subjects			
Adolescents (12-17 years)	4		
Age continuous			
age of patients in years (mean value)			
Units: years			
arithmetic mean			
full range (min-max)	-		
Gender categorical			
gender of the patients			
Units: Subjects			
Female	4		
Male	0		

End points

End points reporting groups

Reporting group title	3x2 verum
Reporting group description: patient received 3x2 tbl a day verum	
Reporting group title	3x1 verum
Reporting group description: patients received 3x1 tbl a day verum and 3x1 tbl a day placebo	
Reporting group title	placebo
Reporting group description: patients received 3x2 tbl a day placebo	

Primary: Change from baseline of CDRS-R at week 6

End point title	Change from baseline of CDRS-R at week 6[1]

End point description:

Note: Due to insufficient enrollment only safety-relevant data were evaluated. There were only data of 5 enrolled patients. Of these, one patient was a screening failure and two patients were drop outs. So there were complete data for 2 patients only.
Therefore, the originally planned evaluation of the efficacy data has had to be abandoned.

End point type	Primary

End point timeframe:

from baseline of CDRS-R at week 6

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: Due to insufficient enrollment only safety-relevant data were evaluated. There were only data of 5 enrolled patients. Of these, one patient was a screening failure and two patients were drop outs. So there were complete data for 2 patients only.
Therefore, the originally planned evaluation of the efficacy data has had to be abandoned.

End point values	3x2 verum	3x1 verum	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: score points				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[2] - Therefore, the originally planned evaluation of the efficacy data has had to be abandoned.

[3] - Therefore, the originally planned evaluation of the efficacy data has had to be abandoned.

[4] - Therefore, the originally planned evaluation of the efficacy data has had to be abandoned.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs should be recorded from the time the subject provides informed consent to the last visit. Each SAE is followed up until complete recovery or the reasons for AE are identified, but the follow up ends 4 weeks after termination of study at latest.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	3x2 verum
Reporting group description:	
patient received 3x2 tbl a day verum	
Reporting group title	3x1 verum
Reporting group description:	
patients received 3x1 tbl a day verum and 3x1 tbl a day placebo	
Reporting group title	placebo
Reporting group description:	
patients received 3x2 tbl a day placebo	

Serious adverse events	3x2 verum	3x1 verum	placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	3x2 verum	3x1 verum	placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	1 / 1 (100.00%)	0 / 1 (0.00%)
Nervous system disorders			
recurrent headache			
subjects affected / exposed	0 / 2 (0.00%)	1 / 1 (100.00%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			

increased appetite			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
suicidal ideations			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 May 2013	The amendments to the documents (protocol and IB) resulting from claims by leading ethics commission (ffEK).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
10 February 2014	The clinical examination had to be canceled due to insufficient recruitment to 10/02/2014.	-

Notes:

Limitations and caveats

None reported