Clinical trial results:
Pregabalin for anxiety comorbidity in patients with schizophrenia (PACS)
- A Double-blinded Randomized Placebo Controlled Trial

Summary

EudraCT number	2010-024488-42
Trial protocol	DK
Global end of trial date	15 August 2016

Results information

Result version number	v1 (current)
This version publication date	30 September 2021
First version publication date	30 September 2021

Trial information

Trial identification

Sponsor protocol code	2010-024488-42-PACS

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01496690
WHO universal trial number (UTN)	-
Other trial identifiers	The North Dk Region Comm. on Health Res. Ethics: N20100097

Notes:

Sponsors

Sponsor organisation name	Aalborg Psychiatric Hospital
Sponsor organisation address	Mølleparkvej 10, Aalborg, Denmark, 9000
Public contact	Centre for Psychosis Research, Aalborg University Hospital, Aalborg Psychiatric Hospital, 0045 29323543, ole.schjerning@rsyd.dk
Scientific contact	Centre for Psychosis Research, Aalborg University Hospital, Aalborg Psychiatric Hospital, 0045 29323543, ole.schjerning@rsyd.dk

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	01 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 August 2016
Global end of trial reached?	Yes
Global end of trial date	15 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect and tolerability of pregabalin for schizophrenic patients that suffer from comorbid anxiety.

Protection of trial subjects:

All participants provided written informed consent to participation.
This study was performed in accordance with the ICH-CGP guidelines and the Declaration of Helsinki. The Local Ethics Committee, the Danish Health Authority and the Danish Data Protection Agency approved the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2012
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	Denmark: 54
Worldwide total number of subjects	54
EEA total number of subjects	54

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)	54
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from all five regions of Denmark. First patient was included at 5th of March 2012 and last patient ended the study at 15th of August 2016. The study was ended before sample size goal was met due to failure in accessing eligible patients.

Pre-assignment

Screening details:

Patients aged 18 to 65 years with a diagnosis of schizophrenia (ICD-10: F20.0 to F20.3 or F20.9). No changes in primary psychopharmacologic treatment (antipsychotics, antidepressants and sedatives) for at least 4 weeks.
Severity of anxiety was measured using the Hamilton Anxiety Scale. Patients with a total score above 15 were included.

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, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Randomization was done in blocks with variable block size (4, 6 and 8) to maintain an equal allocation of patients over time. Randomization sequence was generated by the Hospital Pharmacy, Aalborg University Hospital, Aalborg, Denmark. All research staff and patientswere blinded to treatment allocation. Pregabalin capsules and placebo capsules were identical and provided by Pfizer Denmark.

Arms

Are arms mutually exclusive?	Yes
Arm title	Pregabalin

Arm description:

Active treatment

Arm type	Active comparator
Investigational medicinal product name	Pregabalin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pregabalin/placebo was initiated at 75 mg/d. After one week, dosage was increased to 150 mg/d and a flexible dosage regiment allowing weekly increments by 150 mg/d, up to a maximum of 600 mg/d — depending on effect and tolerability. Dosages ≥450 mg/d were divided in two doses. Compliance was calculated after 4 and 8 weeks.

Arm title	Placebo

Arm description:

Placebo

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pregabalin/placebo was initiated at 75 mg/d. After one week, dosage was increased to 150 mg/d and a flexible dosage regiment allowing weekly increments by 150 mg/d, up to a maximum of 600 mg/d — depending on effect and tolerability. Dosages ≥450 mg/d were divided in two doses. Compliance was calculated after 4 and 8 weeks.

Number of subjects in period 1	Pregabalin	Placebo
Started	28	26
Completed	22	22
Not completed	6	4
Consent withdrawn by subject	-	1
Adverse event, non-fatal	3	2
Compliance below 70%	3	-
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Pregabalin
Reporting group description:	
Active treatment	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Reporting group values	Pregabalin	Placebo	Total
Number of subjects	28	26	54
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)	28	26	54
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	11	7	18
Male	17	19	36

Subject analysis sets	
Subject analysis set title	End trial analysis
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Difference between ratings at baseline and after 8 weeks of treatment on the Hamilton Anxiety Scale.	

Reporting group values	End trial analysis		
Number of subjects	54		
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			

Gender categorical Units: Subjects			
Female	18		
Male	36		

End points

End points reporting groups

Reporting group title	Pregabalin
Reporting group description: Active treatment	
Reporting group title	Placebo
Reporting group description: Placebo	
Subject analysis set title	End trial analysis
Subject analysis set type	Intention-to-treat
Subject analysis set description: Difference between ratings at baseline and after 8 weeks of treatment on the Hamilton Anxiety Scale.	

Primary: HAM-A14

End point title	HAM-A14
End point description:	
End point type	Primary
End point timeframe: 8 weeks treatment	

End point values	Pregabalin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	26		
Units: HAM-A14 scale units	28	26		

Statistical analyses

Statistical analysis title	Change in HAM-A14 score
Statistical analysis description: Difference between HAM-A14 ratings at baseline and after 8 weeks of treatment.	
Comparison groups	Pregabalin v Placebo
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	equivalence
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	5.9

Variability estimate	Standard deviation

Secondary: HAM-A6	
End point title	HAM-A6
End point description:	
End point type	Secondary
End point timeframe:	
After 8 weeks treatment	

End point values	Pregabalin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	26		
Units: HAM-A6 score	28	26		

Statistical analyses

Statistical analysis title	Change in HAM-A6 scores
Comparison groups	Pregabalin v Placebo
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	equivalence
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	4
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

8 weeks of treatment

Assessment type	Systematic

Dictionary used

Dictionary name	None
Dictionary version	0

Reporting groups

Reporting group title	Pregabalin

Reporting group description:

Pregabalin/placebo was initiated at 75 mg/d. After one week, dosage was increased to 150 mg/d and a flexible dosage regiment allowing weekly increments by 150 mg/d, up to a maximum of 600 mg/d — depending on effect and tolerability. Dosages ≥450 mg/d were divided in two doses. Compliance was calculated after 4 and 8 weeks.

Reporting group title	Placebo

Reporting group description:

Pregabalin/placebowas initiated at 75 mg/d. After oneweek, dosage was increased to 150 mg/d and a flexible dosage regiment allowing weekly increments by 150 mg/d, up to a maximum of 600 mg/d — depending on effect and tolerability. Dosages ≥450 mg/d were divided in two doses. Compliance was calculated after 4 and 8 weeks.

Serious adverse events	Pregabalin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 28 (10.71%)	1 / 26 (3.85%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Psychiatric disorders			
Worsening of hallucinations			
subjects affected / exposed	3 / 28 (10.71%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt	Additional description: Suicide attempt using overdose of benzodiazepines		
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	
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 %

Non-serious adverse events	Pregabalin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 28 (100.00%)	26 / 26 (100.00%)	
Cardiac disorders			
Palpitations			
subjects affected / exposed	5 / 28 (17.86%)	4 / 26 (15.38%)	
occurrences (all)	5	4	
Nervous system disorders			
Dizziness			
subjects affected / exposed	11 / 28 (39.29%)	5 / 26 (19.23%)	
occurrences (all)	11	5	
Increased fatiguability			
subjects affected / exposed	9 / 28 (32.14%)	6 / 26 (23.08%)	
occurrences (all)	9	6	
Sedation			
subjects affected / exposed	5 / 28 (17.86%)	4 / 26 (15.38%)	
occurrences (all)	5	4	
Dystonia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Rigidity			
subjects affected / exposed	3 / 28 (10.71%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Hypokinesia			
subjects affected / exposed	3 / 28 (10.71%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Hyperkinesia			
subjects affected / exposed	5 / 28 (17.86%)	1 / 26 (3.85%)	
occurrences (all)	5	1	
Tremor			
subjects affected / exposed	3 / 28 (10.71%)	3 / 26 (11.54%)	
occurrences (all)	3	3	
Akathisia			
subjects affected / exposed	7 / 28 (25.00%)	3 / 26 (11.54%)	
occurrences (all)	7	3	
Epileptic seizures			

subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Paresthesia			
subjects affected / exposed	3 / 28 (10.71%)	2 / 26 (7.69%)	
occurrences (all)	3	2	
Dizziness postural			
subjects affected / exposed	6 / 28 (21.43%)	7 / 26 (26.92%)	
occurrences (all)	6	7	
Headache			
subjects affected / exposed	6 / 28 (21.43%)	6 / 26 (23.08%)	
occurrences (all)	6	6	
Eye disorders			
Accommodation disorder			
subjects affected / exposed	5 / 28 (17.86%)	1 / 26 (3.85%)	
occurrences (all)	5	1	
Gastrointestinal disorders			
Increased salivation			
subjects affected / exposed	5 / 28 (17.86%)	2 / 26 (7.69%)	
occurrences (all)	5	2	
Dryness of mouth			
subjects affected / exposed	4 / 28 (14.29%)	5 / 26 (19.23%)	
occurrences (all)	4	5	
Nausea			
subjects affected / exposed	5 / 28 (17.86%)	6 / 26 (23.08%)	
occurrences (all)	5	6	
Diarrhoea			
subjects affected / exposed	6 / 28 (21.43%)	4 / 26 (15.38%)	
occurrences (all)	6	4	
Constipation			
subjects affected / exposed	3 / 28 (10.71%)	3 / 26 (11.54%)	
occurrences (all)	3	3	
Reproductive system and breast disorders			
Increased sexual desire			
subjects affected / exposed	2 / 28 (7.14%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Diminished sexual desire			

subjects affected / exposed	6 / 28 (21.43%)	2 / 26 (7.69%)	
occurrences (all)	6	2	
Orgasmic dysfunction			
subjects affected / exposed	7 / 28 (25.00%)	3 / 26 (11.54%)	
occurrences (all)	7	3	
Skin and subcutaneous tissue disorders			
Increased tendency to sweating			
subjects affected / exposed	2 / 28 (7.14%)	1 / 26 (3.85%)	
occurrences (all)	2	1	
Rash			
subjects affected / exposed	3 / 28 (10.71%)	1 / 26 (3.85%)	
occurrences (all)	3	1	
Pruritus			
subjects affected / exposed	2 / 28 (7.14%)	1 / 26 (3.85%)	
occurrences (all)	2	1	
Photosensitivity reaction			
subjects affected / exposed	3 / 28 (10.71%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Increased pigmentation			
subjects affected / exposed	4 / 28 (14.29%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Psychiatric disorders			
Concentration difficulties			
subjects affected / exposed	4 / 28 (14.29%)	3 / 26 (11.54%)	
occurrences (all)	4	3	
Failing memory			
subjects affected / exposed	6 / 28 (21.43%)	5 / 26 (19.23%)	
occurrences (all)	6	5	
Depression			
subjects affected / exposed	5 / 28 (17.86%)	9 / 26 (34.62%)	
occurrences (all)	5	9	
Tension			
subjects affected / exposed	4 / 28 (14.29%)	4 / 26 (15.38%)	
occurrences (all)	4	4	
Increased duration of sleep			

subjects affected / exposed	15 / 28 (53.57%)	2 / 26 (7.69%)	
occurrences (all)	15	2	
Reduced duration of sleep			
subjects affected / exposed	2 / 28 (7.14%)	3 / 26 (11.54%)	
occurrences (all)	2	3	
Increased dream activity			
subjects affected / exposed	6 / 28 (21.43%)	3 / 26 (11.54%)	
occurrences (all)	6	3	
Emotional indifference			
subjects affected / exposed	4 / 28 (14.29%)	2 / 26 (7.69%)	
occurrences (all)	4	2	
Renal and urinary disorders			
Micturition disorder			
subjects affected / exposed	5 / 28 (17.86%)	4 / 26 (15.38%)	
occurrences (all)	5	4	
Polyuria			
subjects affected / exposed	9 / 28 (32.14%)	2 / 26 (7.69%)	
occurrences (all)	9	2	
Metabolism and nutrition disorders			
Weight gain poor			
subjects affected / exposed	24 / 28 (85.71%)	9 / 26 (34.62%)	
occurrences (all)	24	9	
Weight loss			
subjects affected / exposed	3 / 28 (10.71%)	7 / 26 (26.92%)	
occurrences (all)	3	7	

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/28919128