



Clinical trial results:

NEUPRO OL, Efficacy profile of Neurexan® in an experimental acute stress setting – an explorative open-label study in healthy probands

Summary

EudraCT number	2012-002359-40
Trial protocol	DE
Global end of trial date	04 April 2013

Results information

Result version number	v1 (current)
This version publication date	28 October 2017
First version publication date	28 October 2017
Summary attachment (see zip file)	C1202 NEUPRO Open label study (Neurexan) (C1202_20131212_C1202_NEUPRO_OL_Synopsis_CSR_03Dec2013_redacted.pdf)

Trial information

Trial identification

Sponsor protocol code	C1202
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01703832
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biologische Heilmittel Heel GmbH
Sponsor organisation address	Dr.-Reckeweg-Str. 2-4, Baden-Baden, Germany, 76532
Public contact	Biologische Heilmittel Heel GmbH, Biologische Heilmittel Heel GmbH, +49 7221-501-0, info@heel.com
Scientific contact	Biologische Heilmittel Heel GmbH, Biologische Heilmittel Heel GmbH, +49 7221-501-0, info@heel.com

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	04 April 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 April 2013
Global end of trial reached?	Yes
Global end of trial date	04 April 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is the efficacy of Neurexan® on tension and nervousness perception using visual analogue scales (VAS) when study participants undergo an emotional stressful condition as compared to natural course. The test method for this study is the TSST protocol.

Protection of trial subjects:

Routine monitoring was performed to verify that rights and well being of participants were protected.

Background therapy:

8 subjects took contraceptives (5 in the Neurexan Group, 3 in the Placebo Group)

Evidence for comparator: -

Actual start date of recruitment	12 October 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	Germany: 65
Worldwide total number of subjects	65
EEA total number of subjects	65

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

Subject disposition

Recruitment

Recruitment details:

Recruitment was carried out in 2 outpatient clinics in Germany (Marburg and Essen).

Pre-assignment

Screening details:

Telephone pre-screening was carried out and individuals received gross Information about the study. If they were suited for study participation an appointment for the medical and psychological screening was made.

Interested volunteers were invited to the study site for the 1st visit and received oral and written Information about study and ICF.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Neurexan group

Arm description:

33 participants were randomized to Neurexan. One premature terminator could not be evaluated for primary efficacy, so 32 participants in the Neurexan group formed the full analysis Set for analysis of efficacy. All randomised subjects were included in the analysis of safety.

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

Dosage and administration details:

One Neurexan tablet contains: 0.6 mg Avena sativa (dil. D2), 0.6 mg Coffea arabica (dil. D12), 0.6 mg Passiflora incarnata (dil. D2), 0.6 mg Zincum isovalerianum (dil. D4), lactose monohydrate and magnesium stearate

Route of administration: oral

Total administered: 6 tablets (over a period of 2.5 hours - one tablet every 30 minutes)

Arm title	Natoural course group
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Arm description:

All of the 32 participants randomised to the Natural Course group formed the full analysis set for analysis of efficacy and safety.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Neurexan group	Natoural course group
Started	33	32
Completed	32	32
Not completed	1	0
Consent withdrawn by subject	1	-

Baseline characteristics

Reporting groups

Reporting group title	Neurexan group
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Reporting group description:

33 participants were randomized to Neurexan. One premature terminator could not be evaluated for primary efficacy, so 32 participants in the Neurexan group formed the full analysis Set for analysis of efficacy. All randomised subjects were included in the analysis of safety.

Reporting group title	Natoural course group
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Reporting group description:

All of the 32 participants randomised to the Natural Course group formed the full analysis set for analysis of efficacy and safety.

Reporting group values	Neurexan group	Natoural course group	Total
Number of subjects	33	32	65
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)	33	32	65
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	42.6	41.3	-
standard deviation	± 8.4	± 8.3	-
Gender categorical			
Units: Subjects			
Female	17	17	34
Male	16	15	31
Ethnic origin			
Units: Subjects			
white	33	32	65
Body Mass Index (BMI)			
Units: kg/m2			
arithmetic mean	24.47	23.11	-
standard deviation	± 2.76	± 2.83	-
Trier Inventory for Chronic Stress - screening scale of chronic stress (SSCS)			
Includes scores from five scales (chronic worrying, work and social overload, excessive demands and lack of acceptance).			
Units: score points			
median	8	9.5	-
full range (min-max)	0 to 19	1 to 23	-
Global Severity Index (GSI) of			

psychological distress			
derived from Symptom Checklist 90			
Units: score points			
median	0.133	0.189	
full range (min-max)	0 to 0.82	0 to 1.21	-
Screening height			
Units: cm			
arithmetic mean	175	177.2	
standard deviation	± 9.7	± 10.7	-
Screening weight			
Units: kg			
arithmetic mean	75.35	73.04	
standard deviation	± 12.89	± 13.81	-

End points

End points reporting groups

Reporting group title	Neurexan group
Reporting group description: 33 participants were randomized to Neurexan. One premature terminator could not be evaluated for primary efficacy, so 32 participants in the Neurexan group formed the full analysis Set for analysis of efficacy. All randomised subjects were included in the analysis of safety.	
Reporting group title	Natoural course group
Reporting group description: All of the 32 participants randomised to the Natural Course group formed the full analysis set for analysis of efficacy and safety.	
Subject analysis set title	Essen Neurexan group
Subject analysis set type	Sub-group analysis
Subject analysis set description: The secondary endpoint "Change in natural killer (NK) cells" was analysed in the Essen subgroup only.	
Subject analysis set title	Essen Natoural course group
Subject analysis set type	Sub-group analysis
Subject analysis set description: The secondary endpoint "Change in natural killer (NK) cells" was analysed in the Essen subgroup only.	

Primary: Tension

End point title	Tension
End point description: Tension was self-assessed by the participants on a 0 to 100 millimeter (mm) Visual Analogue Scale (VAS), ranging from 0="not at all" to 100="highly", before and after a stress test. The measurements started 30 min before intake of Neurexan or natural course and were repeated until 100 minutes after the end of the stress test. The total stress was then summarized with the Area under the curve (AUC) method. AUC of VAS Tension value was measured from -210 min to +100 min.	
End point type	Primary
End point timeframe: 30 min before first intake of Neurexan or natural course until 100 minutes after end of the stress test, i.e.: -210 min, -180 min, -150 min, -120 min, -90 min, -60 min, -30 min, -15 min, 0 min, +15 min, +30 min, +45 min, +60 min, +75 min, +100 min	

End point values	Neurexan group	Natoural course group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: mm*min				
median (full range (min-max))	3089.4 (40 to 20940)	3253.4 (308 to 19305)		

Statistical analyses

Statistical analysis title	Descriptive statistics
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Statistical analysis description:

Standard descriptive statistics were calculated for continuous variables. All analyses were performed

using Version 9.1.3 or later of SAS Software.

Comparison groups	Neurexan group v Natoural course group
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1233
Method	ANCOVA
Parameter estimate	LS-Mean Difference
Point estimate	752.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-210.6
upper limit	1715.3
Variability estimate	Standard error of the mean
Dispersion value	481.2

Primary: Nervousness

End point title	Nervousness
End point description:	
Nervousness was self-assessed by the participants on a 0 to 100 millimeter (mm) Visual Analogue Scale (VAS), ranging from 0="not at all" to 100="highly", before and after a stress test. The measurements started 30 min before first intake of Neurexan or natoural course and were repeated until 100 minutes after the end of the stress test.	
The total stress was then summarized with the Area under the curve (AUC) method. AUC of VAS Nervousness value was measured from -210 min to +100 min.	
End point type	Primary
End point timeframe:	
30 min before first intake of Neurexan or natoural course until 100 minutes after end of the stress test, i.e.: -210 min, -180 min, -150 min, -120 min, -90 min, -60 min, -30 min, -15 min, 0 min, +15 min, +30 min, +45 min, +60 min, +75 min, +100 min	

End point values	Neurexan group	Natoural course group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: mm*min				
median (full range (min-max))	2377.3 (12 to 9071)	3426.8 (329 to 14898)		

Statistical analyses

Statistical analysis title	Descriptive statistics
Statistical analysis description:	
Standard descriptive statistics were calculated for continuous variables. All analyses were performed using Version 9.1.3 or later of SAS Software.	
Comparison groups	Neurexan group v Natoural course group

Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5153
Method	ANCOVA
Parameter estimate	LS-Mean Difference
Point estimate	334.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-687.6
upper limit	1356.1
Variability estimate	Standard error of the mean
Dispersion value	510.7

Secondary: Alpha amylase

End point title	Alpha amylase
End point description:	
The stress biomarker salivary alpha amylase was measured before and after a stress test. The measurements started 60 minutes before stress test and were repeated until 100 minutes after the end of the stress test.	
End point type	Secondary
End point timeframe:	
60 minutes before until 100 minutes after stress test, i.e.: -60 min, +15 min, +45 min, +100 min	

End point values	Neurexan group	Natoural course group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32 ^[1]	32		
Units: IU/ml				
median (full range (min-max))				
-60 min	155.6 (21.6 to 594.86)	133.2 (11.5 to 591.83)		
+15 min	242.8 (28.19 to 620.26)	204.9 (9.82 to 819.87)		
+45 min	171.3 (21.04 to 786.54)	138.6 (9.61 to 812.83)		
+100 min	195.8 (17.35 to 597.39)	144 (8.02 to 509.27)		

Notes:

[1] - Parameter was measured in only 31 participants at timepoint -60 min.

Statistical analyses

No statistical analyses for this end point

Secondary: Saliva cortisol

End point title	Saliva cortisol
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End point description:

The stress biomarker saliva cortisol was measured before and after a stress test. The measurements started 60 minutes before stress test and were repeated until 100 minutes after the end of the stress test.

End point type	Secondary
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End point timeframe:

60 minutes before until 100 minutes after stress test, i.e.: -60 min, +15 min, +45 min, +100 min

End point values	Neurexan group	Natoural course group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32 ^[2]	32		
Units: nmol/l				
median (full range (min-max))				
-60 min	7.9 (1.58 to 27.64)	8.1 (2.84 to 26.39)		
+15 min	20.3 (2.46 to 121.11)	19.8 (3.37 to 112.89)		
+45 min	18.8 (1.22 to 65.42)	20.6 (2.59 to 33.61)		
+100 min	8.6 (1.77 to 24.89)	9.4 (3.44 to 89.56)		

Notes:

[2] - Parameter was measured in only 31 participants at timepoint -60 min.

Statistical analyses

No statistical analyses for this end point

Secondary: Adrenocorticotrophic Hormone (ACTH)

End point title	Adrenocorticotrophic Hormone (ACTH)
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End point description:

The stress biomarker Adrenocorticotrophic Hormone was measured before and after a stress test. The measurements started 60 minutes before stress test and were repeated until 100 minutes after the end of the stress test.

End point type	Secondary
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End point timeframe:

60 minutes before until 100 minutes after stress test, i.e.: -60 min, +15 min, +45 min, +100 min

End point values	Neurexan group	Natoural course group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31 ^[3]	24		
Units: ng/l				
median (full range (min-max))				
-60 min	20.8 (6.07 to 283.81)	20 (7.95 to 112.99)		
+15 min	35.4 (13.38 to 116.92)	31 (11.36 to 158.12)		

+45 min	20.4 (9.05 to 55.69)	20.6 (7.51 to 84.08)		
+100 min	11.8 (6.99 to 32.99)	13.7 (3.3 to 31.58)		

Notes:

[3] - Parameter was measured in only 30 participants at timepoint -60 min

Statistical analyses

No statistical analyses for this end point

Secondary: Epinephrine

End point title	Epinephrine
End point description: The stress biomarker epinephrine (adrenaline) measured before and after a stress test. The measurements started 60 minutes before stress test and were repeated until 100 minutes after the end of the stress test.	
End point type	Secondary
End point timeframe: 60 minutes before until 100 minutes after stress test, i.e.: -60 min, +15 min, +45 min, +100 min	

End point values	Neurexan group	Natoural course group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	23		
Units: ng/l				
median (full range (min-max))				
-60 min	44.6 (10 to 108)	37 (11 to 98.6)		
+15 min	35.4 (10 to 146)	31 (10 to 88.4)		
+45 min	37.3 (10 to 105)	32 (9.1 to 95.5)		
+100 min	29.8 (0 to 87.7)	33 (10 to 104)		

Statistical analyses

No statistical analyses for this end point

Secondary: Norepinephrine

End point title	Norepinephrine
End point description: The stress biomarker norepinephrine was measured before and after a stress test. The measurements started 60 minutes before stress test and were repeated until 100 minutes after the end of the stress test.	
End point type	Secondary
End point timeframe: 60 minutes before until 100 minutes after stress test, i.e.: -60 min, +15 min, +45 min, +100 min	

End point values	Neurexan group	Natoural course group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	23		
Units: ng/l				
median (full range (min-max))				
-60 min	484.5 (249 to 923)	457 (195 to 797)		
+15 min	575.5 (299 to 1128)	529 (279 to 1688)		
+45 min	458 (220 to 889)	459 (223 to 858)		
+100 min	467 (269 to 938)	372 (189 to 839)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma cortisol

End point title	Plasma cortisol
End point description:	
The stress biomarker plasma cortisol was measured before and after a stress test. The measurements started 60 minutes before stress test and were repeated until 100 minutes after the end of the stress test.	
End point type	Secondary
End point timeframe:	
60 minutes before until 100 minutes after stress test, i.e.: -60 min, +15 min, +45 min, +100 min	

End point values	Neurexan group	Natoural course group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	24		
Units: nmol/l				
median (full range (min-max))				
-60 min	365.9 (105.11 to 917.95)	337.6 (125.51 to 836.49)		
+15 min	554.3 (72.19 to 971.2)	544.3 (124.52 to 942.52)		
+45 min	466.8 (73.66 to 842.18)	506.8 (121.6 to 815.16)		
+100 min	285.1 (83.99 to 735.4)	285.1 (136.69 to 637.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Natural killer cells

End point title	Change in Natural killer cells
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End point description:

The Natural Killer (NK) Cells as immune cells and stress biomarkers were measured before and after a stress test. The measurements started 60 minutes before stress test and were repeated until 100 minutes after the end of the stress test.

End point type	Secondary
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End point timeframe:

60 minutes before until 100 minutes after stress test, i.e.: -60 min, +15 min, +45 min, +100 min

End point values	Essen Neurexan group	Essen Natoural course group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	12		
Units: % of lymphocytes				
median (full range (min-max))				
-60 min	11.8 (5.8 to 22.6)	11.2 (5.6 to 16.5)		
+15 min	21.3 (9.8 to 28.1)	17.7 (10.1 to 26.2)		
+45 min	11.6 (4.6 to 14.8)	8.6 (4.3 to 12.7)		
+100 min	11.1 (6.1 to 18.2)	7.8 (4 to 20.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Systolic blood presssure

End point title	Systolic blood presssure
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End point description:

Systolic blood pressure was measured before and after a stress test by continuous cardiovascular recording. The measurements started 30 minutes before stress test and were repeated until 45 minutes after the end of the stress test.

End point type	Secondary
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End point timeframe:

30 minutes before until 45 minutes after stress test, i.e.: -15 min, 0 min, +15 min, +45 min

End point values	Neurexan group	Natoural course group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: mmHg				
median (full range (min-max))				
-15 min	120.5 (86 to 175)	123.5 (95 to 147)		
0 min	131 (98 to 204)	136.5 (96 to 171)		
+15 min	123 (92 to 161)	128.5 (86 to 165)		
+45 min	121 (77 to 180)	122 (91 to 160)		

Statistical analyses

No statistical analyses for this end point

Secondary: Diastolic blood pressure

End point title	Diastolic blood pressure
End point description: Diastolic blood pressure was measured before and after a stress test by continuous cardiovascular recording. The measurements started 30 minutes before stress test and were repeated until 45 minutes after the end of the stress test.	
End point type	Secondary
End point timeframe: 30 minutes before until 45 minutes after stress test, i.e.: -15 min, 0 min, +15 min, +45 min	

End point values	Neurexan group	Natoural course group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: mmHg				
median (full range (min-max))				
-15 min	78 (51 to 120)	79 (56 to 103)		
0 min	83.5 (59 to 138)	88.5 (60 to 114)		
+15 min	81.5 (54 to 115)	83 (54 to 109)		
+45 min	78 (40 to 124)	81 (41 to 109)		

Statistical analyses

No statistical analyses for this end point

Secondary: Heart rate

End point title	Heart rate
End point description:	
Heart rate was measured before and after a stress test by continuous cardiovascular recording. The measurements started 30 minutes before stress test and were repeated until 45 minutes after the end of the stress test.	
End point type	Secondary
End point timeframe:	
30 minutes before until 45 minutes after stress test, i.e.: -15 min, 0 min, +15 min, +45 min	

End point values	Neurexan group	Natoural course group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: beats per minute				
median (full range (min-max))				
-15 min	67 (55 to 96)	69 (49 to 98)		
0 min	87 (67 to 135)	83 (56 to 125)		
+15 min	68 (54 to 90)	71 (44 to 93)		
+45 min	68 (56 to 96)	72 (48 to 92)		

Statistical analyses

No statistical analyses for this end point

Secondary: Modified somatic SCL90

End point title	Modified somatic SCL90
End point description:	
The SCL90 has 90 items and covers dimensions like depression, somatization, obsessive-compulsive disorder, social insecurity, anxiety, phobic anxiety, aggression/hostility, paranoid ideation, psychoticism. A new instrument covering potential somatic stress consequences was used in this study, the modified somatic SCL90 that uses the SCL90 somatization items, but instead of a 7 day timeframe asking for "now" (current state). The corresponding items from SCL90 were: 1, 4, 12, 27, 40, 42, 48, 49, 52, 53, 56, 58 and the introductory question had to be: "How much do you currently suffer from..." ("Wie sehr leiden Sie momentan unter:").	
End point type	Secondary
End point timeframe:	
210 minutes before and 100 minutes after stress test, i.e: -210 min, +100 min	

End point values	Neurexan group	Natoural course group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: score points				
median (full range (min-max))				
-210 min	0.042 (0 to 0.67)	0.083 (0 to 1.08)		

+100 min	0 (0 to 0.5)	0 (0 to 0.33)		
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Statistical analyses

No statistical analyses for this end point

Secondary: State anxiety and stress perception measured by State-Trait

End point title	State anxiety and stress perception measured by State-Trait
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End point description:

State anxiety and stress perception were measured by State-Trait Anxiety Inventory X1 before and after a stress test. The measurements took place 90 minutes before stress test and were repeated 15 and 100 minutes after the end of the stress test.

End point type	Secondary
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End point timeframe:

90 minutes before stress test and 15 and 100 minutes after the end of the stress test, i.e.: -90 min, +15 min, +100 min

End point values	Neurexan group	Natoural course group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: score points				
median (full range (min-max))				
-90 min	32 (21 to 49)	33 (22 to 43)		
+15 min	51 (33 to 73)	56 (29 to 78)		
+100 min	32 (21 to 43)	32 (20 to 52)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Randomization until individual study end, i.e.: i.e.: -180 min, -150 min, -120 min, -90 min, -60 min, -30min, -15 min, 0 min, +15 min, +30 min, +45 min, +60 min, +75 min, +100 min

Adverse event reporting additional description:

All adverse events that occurred after the participant has received at least one dose of the product under investigation (or same timepoint without intake for natural course) were to be collected and reported

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.1
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Reporting groups

Reporting group title	Neurexan group
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Reporting group description:

33 participants were randomized to Neurexan. One premature terminator could not be evaluated for primary efficacy, so 32 participants in the Neurexan group formed the full analysis Set for analysis of efficacy. All randomised subjects were included in the analysis of safety.

Reporting group title	Natoural course group
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Reporting group description:

All of the 32 participants randomised to the Natural Course group formed the full analysis set for analysis of efficacy and safety.

Serious adverse events	Neurexan group	Natoural course group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)	0 / 32 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Neurexan group	Natoural course group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 33 (12.12%)	3 / 32 (9.38%)	
Investigations			
Alanin aminotransferase increased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			

subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	1 / 32 (3.13%) 1	
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	1 / 33 (3.03%)	1 / 32 (3.13%)	
occurrences (all)	1	1	
Procedural dizziness			
subjects affected / exposed	0 / 33 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Procedural nausea			
subjects affected / exposed	0 / 33 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 33 (3.03%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	1 / 33 (3.03%)	0 / 32 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	1 / 33 (3.03%)	0 / 32 (0.00%)	
occurrences (all)	1	0	

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/17615391>

<http://www.ncbi.nlm.nih.gov/pubmed/16952284>

<http://www.ncbi.nlm.nih.gov/pubmed/8255414>

<http://www.ncbi.nlm.nih.gov/pubmed/19837490>

<http://www.ncbi.nlm.nih.gov/pubmed/4303377>

<http://www.ncbi.nlm.nih.gov/pubmed/5535207>

<http://www.ncbi.nlm.nih.gov/pubmed/10600217>

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