Clinical trial results:
International randomised double-blind placebo-controlled study on the initial treatment of acute mania with methylphenidate

Summary

EudraCT number	2010-023992-24
Trial protocol	DE ES BE HU
Global end of trial date	08 February 2016

Results information

Result version number	v1 (current)
This version publication date	23 July 2020
First version publication date	23 July 2020
Summary attachment (see zip file)	Synopsis MEMAP acc. to ICH E3 (MEMAP_Synopsis_Final1.0_2016-11-18.pdf)

Trial information

Trial identification

Sponsor protocol code	MEMAP1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01541605
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Universität Leipzig
Sponsor organisation address	Ritterstr. 26, Leipzig, Germany, 04109
Public contact	Prof. Dr. Ulrich Hegerl, Department of Psychiatry and Psychotherapy, 49 341 9724530, Ulrich.Hegerl@medizin.uni-leipzig.de
Scientific contact	Prof. Dr. Ulrich Hegerl, Department of Psychiatry and Psychotherapy, 49 341 9724530, Ulrich.Hegerl@medizin.uni-leipzig.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	18 November 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 February 2016
Global end of trial reached?	Yes
Global end of trial date	08 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To test the hypothesis that methylphenidate immediate release given twice daily (BID) is significantly superior to placebo in the treatment of manic symptoms in patients with bipolar disorder after 2.5 days of treatment as assessed by the Young Mania Rating Scale (YMRS).

Protection of trial subjects:

Patients were closely monitored by the treating staff with regard to safety during the course of the trial. This included documentation of (S)AEs as well as trial specific safety parameters.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 August 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	Spain: 23
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Germany: 17
Worldwide total number of subjects	42
EEA total number of subjects	42

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)	40
From 65 to 84 years	2

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

42 patients were recruited for the MEMAP trial

Pre-assignment

Screening details:

NO screening period

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

Blinding implementation details:

Placebo controlled trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Methylphenidate

Arm description:

2.5 day treatment with methylphenidate BID

Arm type	Experimental
Investigational medicinal product name	Medikinet
Investigational medicinal product code	54569.00.00, 6620412.00.00, 54569.01.00
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2.5 day treatment with methylphenidate.
Medication will be administered
at 10.00 and 15.00 h on day 0 - 15 mg methylphenidate
at 09.00 and 15.00 h on day 1 - 20 mg methylphenidate
at 09.00 h on day 2 - 20 mg methylphenidate

Arm title	Placebo

Arm description:

placebo treatment

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

Dosage and administration details:

twice daily

Number of subjects in period 1	Methylphenidate	Placebo
Started	22	20
Completed	22	20

Baseline characteristics

Reporting groups	
Reporting group title	Methylphenidate
Reporting group description:	
2.5 day treatment with methylphenidate BID	
Reporting group title	Placebo
Reporting group description:	
placebo treatment	

Reporting group values	Methylphenidate	Placebo	Total
Number of subjects	22	20	42
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)	22	18	40
From 65-84 years	0	2	2
85 years and over	0	0	0
Adults	0	0	0
Gender categorical Units: Subjects			
Female	9	11	20
Male	13	9	22

Subject analysis sets	
Subject analysis set title	Intention-To-Treat
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients randomized, who got at least one dosage of treatment regardless of protocol violations.	

Reporting group values	Intention-To-Treat		
Number of subjects	42		
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 Adults	40 2		
Gender categorical Units: Subjects			
Female Male	20 22		

End points

End points reporting groups

Reporting group title	Methylphenidate
Reporting group description:	
2.5 day treatment with methylphenidate BID	
Reporting group title	Placebo
Reporting group description:	
placebo treatment	
Subject analysis set title	Intention-To-Treat
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients randomized, who got at least one dosage of treatment regardless of protocol violations.	

Primary: YMRS: severity of manic symptoms

End point title	YMRS: severity of manic symptoms[1]
End point description:	
The primary efficacy measure in this study was the severity of manic symptoms as measured by a clinician-administered mania rating scale, the Young Mania Rating Scale (YMRS) (Young et al, 1978). A YMRS sum score of at least 12 points reflects mania (for further details see Kluge et al, 2013). The primary endpoint was determined after 2.5 days of treatment with methylphenidate or placebo. Analysis of covariance (ANCOVA) was computed in order to analyze differences between methylphenidate and placebo regarding the primary outcome (the mean change from baseline in the sum score of the YMRS at day 2.5), with gender, age and the severity of mania (as reflected by the YMRS total score at baseline) being the covariates.	
End point type	Primary
End point timeframe:	
day 0 to day 2.5 of treatment	
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: The complete statistical analysis can be found in the publication (see link) and in the trial synopsis, uploaded together with the results report.	

End point values	Methylphenidate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	20		
Units: Score				
arithmetic mean (standard deviation)	5.07 (± 11.44)	7.82 (± 6.42)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: start of treatment until day 9 follow-up	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0
Reporting groups	
Reporting group title	Methylphenidate
Reporting group description: Treatment with Methylphenidate	
Reporting group title	Placebo
Reporting group description: Patients treated with placebo	

Serious adverse events	Methylphenidate	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 20 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Methylphenidate	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 22 (40.91%)	2 / 20 (10.00%)	
Vascular disorders			
Hypertension aggravated			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Paraesthesia of scalp			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Headache			

subjects affected / exposed	2 / 22 (9.09%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Tardive dyskinesia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Edema face			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 22 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 22 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Skin rough			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Mental lability symptom			
subjects affected / exposed	0 / 22 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Mania aggravated			
subjects affected / exposed	2 / 22 (9.09%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Mania			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Stiffness			

subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 20 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 January 2013	new trial site change in selection criteria
24 October 2013	extension of trial duration
31 July 2014	change in trial staff extension of trial duration
24 July 2015	addition of a new trial site

Notes:

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/29174864