Clinical trial results:
Open-label Pilot Study of Memantine in Chronic Cough Patients Attending a Specialist Clinic

Summary

EudraCT number	2011-005151-13
Trial protocol	GB
Global end of trial date	14 August 2013

Results information

Result version number	v1 (current)
This version publication date	11 April 2020
First version publication date	11 April 2020

Trial information

Trial identification

Sponsor protocol code	MEM-COUGH-01

Additional study identifiers

ISRCTN number	ISRCTN99941214
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	REC reference: 11/NW/0840

Notes:

Sponsors

Sponsor organisation name	Manchester University NHS Foundation Trust
Sponsor organisation address	29 Grafton Street, Manchester, United Kingdom, M13 9WU
Public contact	Dr. Jacky Smith, 11/NW/0840, +44 1612915879, jacky.smith@manchester.ac.uk
Scientific contact	Dr. Jacky Smith, 11/NW/0840, +44 1612915879, jacky.smith@manchester.ac.uk

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	14 August 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the change in cough frequency in chronic cough patients after treatment with Memantine by assessing 24 hour cough frequency.

Protection of trial subjects:

All potential adverse effects and risks associated with taking part in the trial were fully explained to patients before they decided whether to participate.

It was made clear to patients at the beginning of the trial that although Memantine is a licensed medication it may not be possible for it to be prescribed for them "off-label" once the trial had ended and that treatment would be discontinued at the end of the study even if they had felt some benefit from taking it.

Objective cough monitoring involves patients wearing a digital recording device to capture how much they cough over a 24 hour period. The device records patient's conversations as well as cough sounds which could be heard by trained cough analysis staff. Any conversation recorded in this manner was treated in accordance with the GMC Confidentiality Booklet and the Data Protection Act. This was explained in detail to patients prior to their participation.

Background therapy:

No background therapy.

Evidence for comparator:

This was an open-label study, no comparators were tested.

Actual start date of recruitment	17 January 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	United Kingdom: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	8
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All patients were recruited from the specialist cough clinic held at University Hospital of South Manchester NHS Foundation Trust between February 2013 and August 2013. All patients were required to read the participant information sheet thoroughly prior to providing written consent.

Pre-assignment

Screening details:

17 patients were screened and 14 enrolled. Reasons for 3 screen failures were; uncontrolled hypertension, use of systemic anticholinergic and clinically significant abnormal blood result.
Main criteria for inclusion were diagnosis of idiopathic chronic cough of >8 weeks duration, aged 18 years or over, normal chest x-ray and normal spirometry.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Baseline
Arm description: -	
Arm type	Enrolled
Investigational medicinal product name	No treatment
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Unknown use

Dosage and administration details:

N/A

Number of subjects in period 1	Baseline
Started	14
Completed	14

Period 2

Period 2 title	Treatment Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Memantine

Arm description:

Escalating doses of memantine 10-40mg

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

Dosage and administration details:

10-40mg OD doses escalating weekly if tolerated. Maximum tolerated dose continued for 4 weeks.

Number of subjects in period 2	Memantine
Started	14
Dosed	14
Completed	12
Not completed	2
Adverse event, non-fatal	2

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	14	14	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	57.9		
standard deviation	± 11.8	-	
Gender categorical Units: Subjects			
Female	13	13	
Male	1	1	
Smoking Status Units: Subjects			
Never smoked	11	11	
Ex smoker	3	3	
Cough Type Units: Subjects			
Dry	11	11	
Productive	3	3	
Cough Duration Units: Years			
arithmetic mean	13.7		
standard deviation	± 6.8	-	

End points

End points reporting groups

Reporting group title	Baseline
Reporting group description: -	
Reporting group title	Memantine
Reporting group description:	
Escalating doses of memantine 10-40mg	

Primary: Awake cough frequency

End point title	Awake cough frequency[1]
End point description:	

End point type	Primary
End point timeframe:	
From baseline to end 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: Details of the statistical analysis have not been inputted to the database as the fields are not tailored to this type of study. Two sided paired-sample t-tests were performed to compare post treatment measurements to baseline. There were no statistically significant differences with the p values for daytime cough frequency and total CQLQ score being p=0.141 and p=0.366 respectively.

End point values	Memantine	Baseline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11[2]	13[3]		
Units: coughs per hour				
geometric mean (confidence interval 95%)	30.9 (15.6 to 61.2)	41.1 (22.9 to 73.8)		

Notes:

[2] - 2 participants withdrew, 1 attended final visit with URTI so cough recording was not carried out

[3] - 1 participant did not complete cough recording

Statistical analyses

No statistical analyses for this end point

Secondary: CQLQ Score

End point title	CQLQ Score
End point description:	

End point type	Secondary
End point timeframe:	
From baseline to end of treatment	

End point values	Memantine	Baseline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13[4]	13[5]		
Units: number score				
arithmetic mean (confidence interval 95%)	62.0 (54.3 to 69.7)	64.6 (58.4 to 70.8)		

Notes:

[4] - 1 missing due to questionnaire being completed incorrectly

[5] - 1 missing due to questionnaire being completed incorrectly

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From start of treatment to end of treatment	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	16
Reporting groups	
Reporting group title	Memantine
Reporting group description: Single arm - escalating memantine treatment	

Serious adverse events	Memantine		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Memantine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)		
Nervous system disorders			
Sedation			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Dysarthria			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
General disorders and administration site conditions			

Dizziness subjects affected / exposed occurrences (all)	10 / 14 (71.43%) 10		
Fatigue subjects affected / exposed occurrences (all)	6 / 14 (42.86%) 6		
Somnolence subjects affected / exposed occurrences (all)	5 / 14 (35.71%) 5		
Headache subjects affected / exposed occurrences (all)	5 / 14 (35.71%) 5		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	4 / 14 (28.57%) 4		
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 3		
Constipation subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Diarrhoea subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Respiratory, thoracic and mediastinal disorders			
Haemoptysis subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Cough subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Lung infection subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 May 2012	Substantial Amendment 1.0: At the request of the MHRA, a section was added to the protocol (6.7) to describe and cover concomitant therapies.
26 November 2012	Substantial Amendment 2.0: Changes were 1. The IMP brand was changed from Ebixa to Axura due to sourcing difficulties. 2. Alterations to eligibility wording around definition of child bearing potential and acceptable methods of contraception. 3. Altered eligibility criteria for uncontrolled hypertension with an increase in acceptable limit. 4. Altered wording to eligibility criteria with regards to history of seizures. 5. Altered wording for eligibility with regards to the use of tricyclic antidepressants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported