Clinical trial results:
Antidepressant controlled trial for negative symptoms in schizophrenia (ACTIONS)

Summary

EudraCT number	2009-009235-30
Trial protocol	GB
Global end of trial date	08 December 2014

Results information

Result version number	v1 (current)
This version publication date	13 February 2016
First version publication date	13 February 2016
Summary attachment (see zip file)	ACTIONS final report (ACTIONS final report_updated.docx)

Trial information

Trial identification

Sponsor protocol code	CRO1250

Additional study identifiers

ISRCTN number	ISRCTN42305247
ClinicalTrials.gov id (NCT number)	NCT01032083
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Imperial College
Sponsor organisation address	Exhibition Road, London, United Kingdom, SW7 2AZ
Public contact	Clinical Trials Office, Centre for Mental Health, Imperial College, v.leeson@imperial.ac.uk
Scientific contact	Clinical Trials Office, Centre for Mental Health, Imperial College, v.leeson@imperial.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	01 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 September 2014
Global end of trial reached?	Yes
Global end of trial date	08 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To establish the clinical and cost effectiveness of augmentation of antipsychotic medication with the antidepressant, citalopram, for the management of negative symptoms in schizophrenia.

Protection of trial subjects:

Thorough monitoring of adverse events and participant wellbeing occurred as part of the assessment process. During assessment and testing, breaks were provided to minimise possible fatigue or stress, and if indicated,the assessments were spread over several days.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 August 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 62
Worldwide total number of subjects	62
EEA total number of subjects	62

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)	62
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Individuals were identified from multidisciplinary teams in adult psychiatry in the UK, treating people with schizophrenia as either inpatients or outpatients.

Pre-assignment

Screening details:

Individuals with an established schizophrenic illness characterised by persistent negative symptoms at a criterion level of severity, despite treatment with antipsychotic medication.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	active (citalopram)

Arm description: -

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

Dosage and administration details:

one capsule (20mg) a day for 48 weeks, but at 4 weeks, a participant's clinician had the option to increase the dose to two capsules (40mg) a day for the remainder of the study.

Arm title	placebo

Arm description: -

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

Dosage and administration details:

one capsule a day for 48 weeks, but at 4 weeks, a participant's clinician had the option to increase the dose to two capsules a day for the remainder of the study.

Number of subjects in period 1	active (citalopram)	placebo
Started	30	32
Completed	19	23
Not completed	11	9
Consent withdrawn by subject	11	9

Baseline characteristics

Reporting groups	
Reporting group title	active (citalopram)
Reporting group description: -	
Reporting group title	placebo
Reporting group description: -	

Reporting group values	active (citalopram)	placebo	Total
Number of subjects	30	32	62
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	43.02	45.1	
standard deviation	± 12.3	± 12.3	-
Gender categorical Units: Subjects			
Female	4	10	14
Male	26	22	48

End points

End points reporting groups

Reporting group title	active (citalopram)
Reporting group description: -	
Reporting group title	placebo
Reporting group description: -	

Primary: quality of life

End point title	quality of life
End point description:	
End point type	Primary
End point timeframe:	
12 weeks	

End point values	active (citalopram)	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	25		
Units: quality of life scale score				
number (not applicable)	52	49.5		

Statistical analyses

Statistical analysis title	Difference in 12 week quality of life score
Statistical analysis description:	
Baseline values for variable were included as covariates in regression models and adjusted according to ANCOVA	
Comparison groups	active (citalopram) v placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.17
Method	ANCOVA

Primary: quality of life

End point title	quality of life
End point description:	
End point type	Primary

End point timeframe:
48 weeks

End point values	active (citalopram)	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	20		
Units: quality of life scale score				
number (not applicable)	63.1	54.5		

Statistical analyses

Statistical analysis title	Difference in 48 week quality of life score
Statistical analysis description:	
Baseline values for variable were included as covariates in regression models and adjusted according to ANCOVA	
Comparison groups	active (citalopram) v placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.98
Method	ANCOVA

Primary: negative symptoms

End point title	negative symptoms
End point description:	
End point type	Primary
End point timeframe:	
12 weeks	

End point values	active (citalopram)	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	24		
Units: PANSS negative subscale score				
number (not applicable)	21.5	23		

Statistical analyses

Statistical analysis title	Difference in 12 week negative symptom score

Statistical analysis description:

Baseline values for variable were included as covariates in regression models and adjusted according to ANCOVA

Comparison groups	active (citalopram) v placebo
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.32
Method	ANCOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

9th September 2011 to 8th December 2014

Adverse event reporting additional description:

The Antipsychotic Non-Neurological Side-Effects Rating Scale was enhanced to include additional questions relating to known side-effects of citalopram. The assessment was carried out at each timepoint. Where

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16

Reporting groups

Reporting group title	active (citalopram)
Reporting group description: -	
Reporting group title	placebo

Reporting group description: -

Serious adverse events	active (citalopram)	placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	0 / 32 (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	active (citalopram)	placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 28 (39.29%)	16 / 32 (50.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 28 (3.57%)	5 / 32 (15.63%)	
occurrences (all)	20	4	
Dizziness			
subjects affected / exposed	5 / 28 (17.86%)	2 / 32 (6.25%)	
occurrences (all)	5	3	
Gastrointestinal disorders			

Vomiting subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2	3 / 32 (9.38%) 4	
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	3 / 32 (9.38%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 November 2011	New safety information about citalopram was published by the manufacturer in conjunction with the MHRA in late 2011 with a warning about the risk of QTc prolongation and stating that co-administration of citalopram with medicines that prolong the QT interval (including antipsychotic drugs) was therefore contraindicated. Plasma potassium and magnesium levels were measured at baseline while the ECG QTc interval was measured at baseline, 12, 36 and 48 weeks post study entry for all participants entering the study after the Urgent Safety Measures were implemented.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
18 November 2011	An urgent safety measure agreed with the MHRA on 18th November 2011 was not given approval by the Research Ethics Committee until 15th June 2012. The trial was unable to randomise participants during this time	-

Notes:

Limitations and caveats

None reported