Clinical trial results:
a phase IV, double-blind randomised placebo-controlled, parallel group multi-site trial of sertraline compared to placebo in patients presenting with depressive symptoms in primary care where treatment with SSRIs is uncertain.

What are the indications for Prescribing ANtiDepressants that will leAd to a clinical benefit? PANDA RCT

Summary

EudraCT number	2013-003440-22
Trial protocol	GB
Global end of trial date	31 December 2017

Results information

Result version number	v1 (current)
This version publication date	20 October 2019
First version publication date	20 October 2019
Summary attachment (see zip file)	Results (PANDA_Results.pdf) Results Supplementary Appendix (Results Supplementary Appendix.pdf)

Trial information

Trial identification

Sponsor protocol code	13/0413

Additional study identifiers

ISRCTN number	ISRCTN84544741
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University College London
Sponsor organisation address	Joint Research Office, UCL, Gower Street, , London , United Kingdom, WC1E 6BT
Public contact	Glyn Lewis, University College London, +44 0207 679 9253, glyn.lewis@ucl.ac.uk
Scientific contact	Glyn Lewis, University College London, +44 0207 679 9253, glyn.lewis@ucl.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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 August 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2017
Global end of trial reached?	Yes
Global end of trial date	31 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To investigate the severity and duration of the depressive symptoms that are associated with a clinically important response (compared to placebo) to sertraline in people with depression.
- To investigate quality of life, the economic cost and whether performances on emotional processing tasks are associated with response to treatment with sertraline.

Protection of trial subjects:

People with depression have an increased risk of self-harm and suicide. We therefore had a Suicidal Ideation SOP in place and staff were trained to follow this procedure.
The role of the trial steering committee for this trial was to provide independent oversight of ethical and safety aspects of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 May 2014
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: 655
Worldwide total number of subjects	655
EEA total number of subjects	655

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)	616
From 65 to 84 years	39
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from primary care practices across the UK, in the areas surrounding our four trial sites: Bristol, London, Liverpool and York. Bristol recruited the first participant in January 2015, London in July 2015, Liverpool in December 2015 and York in January 2016

Pre-assignment

Screening details:

Eligible participants were those who: were between the ages of 18 to 74; had presented to primary care with depression or low mood during the past 2 years; had not received antidepressant or anti-anxiety medication in the 8 weeks prior to enrolment in the trial and there was clinical equipoise about the benefits of SSRI medication.

Period 1

Period 1 title	Overall trial period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

- Over encapsulation.

- Randomisation was conducted by PRIMENT CTU using a remote computer-generated code (Sealed Envelope, https://sealedenvelope.com/).

Arms

Are arms mutually exclusive?	Yes
Arm title	Sertraline

Arm description:

one × 50 mg encapsulated sertraline for 1 week followed by two × 50 mg encapsulated sertraline for up to 11 weeks and then for a 2-week tapering period. If participants have not responded to treatment after the 6-week follow-up assessment, the medication can be increased to three × 50 mg encapsulated sertraline or identical placebo in consultation with the PI (Principal Investigator)

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

Dosage and administration details:

one × 50 mg encapsulated sertraline for 1 week followed by two × 50 mg encapsulated sertraline for up to 11 weeks and then for a 2-week tapering period. If participants have not responded to treatment after the 6-week follow-up assessment, the medication can be increased to three × 50 mg encapsulated sertraline.

Arm title	Placebo

Arm description:

Matching placebo

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:
100mg

Number of subjects in period 1	Sertraline	Placebo
Started	326	329
Completed	269	268
Not completed	57	61
Consent withdrawn by subject	57	61

Baseline characteristics

Reporting groups

Reporting group title	Overall trial period

Reporting group description: -

Reporting group values	Overall trial period	Total	
Number of subjects	655	655	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Adults (65-74 years)	0	0	
18-74	655	655	
Gender categorical Units: Subjects			
Female	385	385	
Male	270	270	

End points

End points reporting groups

Reporting group title	Sertraline

Reporting group description:

one × 50 mg encapsulated sertraline for 1 week followed by two × 50 mg encapsulated sertraline for up to 11 weeks and then for a 2-week tapering period. If participants have not responded to treatment after the 6-week follow-up assessment, the medication can be increased to three × 50 mg encapsulated sertraline or identical placebo in consultation with the PI (Principal Investigator)

Reporting group title	Placebo

Reporting group description:

Matching placebo

Primary: outcome at 6 weeks

End point title	outcome at 6 weeks[1]

End point description:

End point type	Primary

End point timeframe:

6 weeks

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: Full details of the statistical analyses are detailed in the attached report.

End point values	Sertraline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	266	284		
Units: PhQ-9	8	9		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
baseline for the final to 12 weeks follow-up	
Adverse event reporting additional description:	
Adverse events were recorded by a structured assessment in the 2, 6 and 12 week follow-up assessments. As this trial was a trial of a licensed medication with a well-established safety profile that is used within its licensed indication, AEs were not recorded from those AEs of special interest included in the follow up assessments.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: See attached report for full details of all Adverse Events.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 April 2015	In response to the NIHR stakeholder review, we further developed the analysis plan and the final version was sited in the section number 14.6, page 46 of the protocol. Amendments to the trial protocol have been made in line with agreed analysis plan.
16 November 2015	Following poor recruitment from practice mailouts and after consultations with PPI we changed the recruitment procedure to allow an additional telephone call to those who failed to respond to initial mailout
21 March 2016	Due to a release of SmPC v7 that mentioned an increased QT interval associated with Sertraline and after discussions with our Sponsor we amended the protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported