Clinical trial results:
Ondansetron for the treatment of IBS with diarrhoea (IBS-D): Identifying the “responder”

Summary

EudraCT number	2008-000623-25
Trial protocol	GB
Global end of trial date	30 June 2011

Results information

Result version number	v1
This version publication date	07 January 2019
First version publication date	07 January 2019
Summary attachment (see zip file)	published paper (Garsed, 2014 Ondansetron trial in IBS-D.pdf)

Trial information

Trial identification

Sponsor protocol code	32492

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00745004
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Nottingham University Hospitals NHS Trust
Sponsor organisation address	Queen's Medical Centre, Clifton Boulevard, Nottingham, United Kingdom, NG7 2UH
Public contact	Professor Robin Spiller, Nottingham University Hospitals NHS Trust, 0115 8231032, robin.spiller@nottingham.ac.uk
Scientific contact	Professor Robin Spiller, Nottingham University Hospitals NHS Trust, 0115 8231032, robin.spiller@nottingham.ac.uk
Sponsor organisation name	Nottingham University Hospitals NHS Trust
Sponsor organisation address	Queen's Medical Centre, Clifton Boulevard, Nottingham, United Kingdom, NG7 2UH
Public contact	Professor Robin Spiller, Nottingham Digestive Diseases Biomedical Research Unit Nottingham Digestive Diseases Centre Unive, 0115 823090, emma.bradley@nottingham.ac.uk
Scientific contact	Professor Robin Spiller, Nottingham Digestive Diseases Biomedical Research Unit Nottingham Digestive Diseases Centre Unive, 0115 8231032, robin.spiller@nottingham.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No	No

1901/2006 apply to this trial?	
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	30 June 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2011
Global end of trial reached?	Yes
Global end of trial date	30 June 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To identify clinical features which will predict response to Ondansetron in clinical practice in patients with IBS symptoms with diarrhoea. using a cross-over design

Protection of trial subjects:

The trial was registered on clinicaltrials.gov (identifier NCT00745004), approved by Nottingham Research Ethics Committee 2 (REC reference number 08/H0408/134) and by the Medicines and Healthcare Regulatory authority (MHRA, London, UK), and conducted according to Good Clinical Practice guidelines.

Background therapy:

none

Evidence for comparator:

placebo was used as no approved therapy for IBS with diarrhoea

Actual start date of recruitment	01 January 2009
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: 120
Worldwide total number of subjects	120
EEA total number of subjects	120

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)	120
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Clinics and public advertisement

Pre-assignment

Screening details:

Screened to exclude coeliac disease, microscopic colitis

Period 1

Period 1 title	first treatment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

overencapsulated identical appearing capsules or ondansetron 4mg

Arms

Are arms mutually exclusive?	Yes
Arm title	placebo

Arm description:

placebo tablets titrated from 1 daily or every other day up to 2 t.d.s

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:

inert filler

Arm title	ondansetron

Arm description:

ondansetron 4mg tablets titrated from 1 daily or every other day up to 2 t.d.s

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

Dosage and administration details:

ondansetron 4mg tablets titrated from 1 daily or every other day up to 2 t.d.s

Number of subjects in period 1	placebo	ondansetron
Started	59	61
Completed	55	54
Not completed	4	7
Consent withdrawn by subject	3	5
Adverse event, non-fatal	-	2
Protocol deviation	1	-

Period 2	
Period 2 title	second treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:
identical appearing capsules

Arms

Are arms mutually exclusive?	Yes
Arm title	ondansetron

Arm description:
Ondansetron titrated from 4mg everyother day to 8mg t.d.s. as needed

Arm type	cross-over design
Investigational medicinal product name	ondansetron
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
4mg ondansetron over encapsulated to all;w blinding

Arm title	placebo

Arm description:
placebo dose titrated from 1 every other day to 2 t.d.s. as needed

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:
capsule oral

Number of subjects in period 2	ondansetron	placebo
Started	55	54
Completed	51	47
Not completed	4	7
Consent withdrawn by subject	3	4
Adverse event, non-fatal	1	3

Baseline characteristics

Reporting groups	
Reporting group title	placebo
Reporting group description:	
placebo tablets titrated from 1 daily or every other day up to 2 t.d.s	
Reporting group title	ondansetron
Reporting group description:	
ondansetron 4mg tablets titrated from 1 daily or every other day up to 2 t.d.s	

Reporting group values	placebo	ondansetron	Total
Number of subjects	59	61	120
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	41.1	40.6	
standard deviation	± 12	± 12	-
Gender categorical Units: Subjects			
Female	41	46	87
Male	18	15	33

End points

End points reporting groups

Reporting group title	placebo
Reporting group description: placebo tablets titrated from 1 daily or every other day up to 2 t.d.s	
Reporting group title	ondansetron
Reporting group description: ondansetron 4mg tablets titrated from 1 daily or every other day up to 2 t.d.s	
Reporting group title	ondansetron
Reporting group description: Ondansetron titrated from 4mg everyother day to 8mg t.d.s. as needed	
Reporting group title	placebo
Reporting group description: placebo dose titrated from 1 every other day to 2 t.d.s. as needed	

Primary: stool consistency

End point title	stool consistency
End point description: average of daily stool form scores using bristol stool form score	
End point type	Primary
End point timeframe: last 2 weeks of treatment	

End point values	placebo	ondansetron	ondansetron	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	61	55	54
Units: bristol stool form score				
number (confidence interval 95%)	4.9 (2.9 to 6.9)	4.0 (1.2 to 6.8)	4.8 (2.8 to 7.0)	3.9 (1.8 to 6.1)

Statistical analyses

Statistical analysis title	analysis
Statistical analysis description: Analysis was carried out with Stata 12. First, intention-to-treat analysis (ITT) was carried out with available data. Second, the data were re-analysed as per protocol (PPA). Baseline variables were analysed by dropout status with t test, Kruskal–Wallis test Garsed K, et al. Gut 2014;63:1617–1625. doi:10.1136/gutjnl-2013-305989 1619 Neurogastroenterology Downloaded from gut.bmj.com on September 3, 2014 - Published by group.bmj.com or $\chi 2$ test for symmetrical, skewed or categorical variable	
Comparison groups	placebo v ondansetron v ondansetron v placebo

Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.6
Variability estimate	Standard deviation
Dispersion value	0.15

Adverse events

Adverse events information	
Timeframe for reporting adverse events: during treatment periods	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	11
Reporting groups	
Reporting group title	ondansetron treatment
Reporting group description: -	
Reporting group title	placebo group
Reporting group description: -	

Serious adverse events	ondansetron treatment	placebo group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 116 (0.00%)	0 / 113 (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: 2 %

Non-serious adverse events	ondansetron treatment	placebo group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 116 (2.59%)	3 / 113 (2.65%)	
General disorders and administration site conditions			
lack of efficacy			
subjects affected / exposed	0 / 116 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	3 / 116 (2.59%)	0 / 113 (0.00%)	
occurrences (all)	3	0	
abdominal pain			
subjects affected / exposed	0 / 116 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	

Musculoskeletal and connective tissue disorders			
back pain			
subjects affected / exposed	0 / 116 (0.00%)	1 / 113 (0.88%)	
occurrences (all)	0	1	

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/24334242