Clinical trial results:
Misoprostol for the Healing of Small Bowel Ulceration in Patients with Obscure Blood Loss while Taking Low-Dose Aspirin or Non-Steroidal Anti-inflammatory Drugs [MASTERS Trial]

Summary

EudraCT number	2013-003187-31
Trial protocol	GB
Global end of trial date	11 October 2017

Results information

Result version number	v1 (current)
This version publication date	11 September 2020
First version publication date	11 September 2020
Summary attachment (see zip file)	Friendly Summary - MASTERS Trial (Friendly Summary-MASTERS Trial.docx)

Trial information

Trial identification

Sponsor protocol code	GN09CA403

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02202967
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	NHS Ayrshire & Arran
Sponsor organisation address	Simpson Street, Kilmarnock, United Kingdom, KA2 0BE
Public contact	Dr A S Taha, NHS Ayrshire & Arran, University Hospital Crosshouse, 44 1563827280, ali.taha1@btinternet.com
Scientific contact	Dr A S Taha, NHS Ayrshire & Arran, University Hospital Crosshouse, 44 1563827280, ali.taha1@btinternet.com
Sponsor organisation name	NHS Greater Glasgow & Clyde R&D Office, Dykebar Hospital
Sponsor organisation address	Grahamston Road, Paisley, United Kingdom, PA2 7DE
Public contact	Dr Maureen Travers, NHS Greater Glasgow & Clyde, 44 141 314 4012, Maureen.Travers@ggc.scot.nhs.uk
Scientific contact	Dr Maureen Travers, NHS Greater Glasgow & Clyde, 44 141 314 4012, Maureen.Travers@ggc.scot.nhs.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	28 November 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 October 2017
Global end of trial reached?	Yes
Global end of trial date	11 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

In cases of iron deficiency anaemia or obscure gastrointestinal bleeding:
To assess the efficacy of an off-patent prostaglandin analogue, misoprostol, in healing of small bowel mucosal damage while continuing to take low-dose aspirin and/ or NSAIDs.

Protection of trial subjects:

Exclusion of women of child-bearing potential if not using reliable contraceptive methods.

Background therapy:

N/A

Evidence for comparator:

Misoprostol is licensed for the healing of peptic ulcers caused by aspirin or non-steroidal anti-inflammatory drugs. Its effect on smal bowel ulcers is not known in users of these drugs.

Actual start date of recruitment	07 January 2016
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: 104
Worldwide total number of subjects	104
EEA total number of subjects	104

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)	80
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment dates: 7 January 2016 - 11 October 2017.

Pre-assignment

Screening details:

We recruited patients (aged ≥18 years) with small bowel ulcers and taking aspirin, NSAIDs, or both for a minimum of 4 weeks. Eligible patients had evidence of obscure gastrointestinal bleeding (iron deficiency anaemia, a decrease in haemoglobin level of ≥20 × 10^3 mg/L, or positive faecal occult blood test) and normal upper endoscopy and colonoscopy

Pre-assignment period milestones

Number of subjects started	104
Number of subjects completed	104

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

Blinding implementation details:

Randomisation was carried out using an interactive voice response system that allocated therapy packs per patient by telephone. The randomisation schedule was computer-generated, using the method of randomised permuted blocks of length 6 without stratification.
Patients, investigators, and assessors were masked to study treatment. Misoprostol and placebo capsules were identical in shape, colour, odour, and taste.

Arms

Are arms mutually exclusive?	Yes
Arm title	Active treatment

Arm description:

patients taking misoprostol

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

Dosage and administration details:

200 ug four times daily

Arm title	Placebo group

Arm description:

Placebo

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Active treatment	Placebo group
Started	52	52
Completed	52	52

Baseline characteristics

Reporting groups	
Reporting group title	Active treatment
Reporting group description: patients taking misoprostol	
Reporting group title	Placebo group
Reporting group description: Placebo	

Reporting group values	Active treatment	Placebo group	Total
Number of subjects	52	52	104
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			
median	68	63	
inter-quartile range (Q1-Q3)	58 to 71	57 to 71	-
Gender categorical Units: Subjects			
Female	22	28	50
Male	30	24	54

End points

End points reporting groups	
Reporting group title	Active treatment
Reporting group description: patients taking misoprostol	
Reporting group title	Placebo group
Reporting group description: Placebo	

Primary: Numbers of patients with fully healed ulcers and erosions at end of the trial

End point title	Numbers of patients with fully healed ulcers and erosions at end of the trial
End point description:	
End point type	Primary
End point timeframe: The end of the study at 8 weeks	

End point values	Active treatment	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50[1]	52[2]		
Units: numbers of patients	27	9		

Notes:

[1] - Two completed patients were excluded from the final analysis because of protocol violation

[2] - correct number

Attachments (see zip file)	Outcomes of MASTERS Trial/MHRA_MASTERS-Primary and

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	Active treatment v Placebo group
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Fisher exact
Parameter estimate	negative binomial regression models
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.5
upper limit	53.9

Secondary: Change in haemoglobin level

End point title	Change in haemoglobin level
End point description:	
End point type	Secondary
End point timeframe:	
8 weeks	

End point values	Active treatment	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	52		
Units: mg/mL				
median (inter-quartile range (Q1-Q3))	136 (121 to 145)	136 (121 to 145)		

Statistical analyses

Statistical analysis title	Multivariable regression analysis
Comparison groups	Active treatment v Placebo group
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.82
Method	multivariable regression
Parameter estimate	Median difference (final values)
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.84
upper limit	4.24

Adverse events

Adverse events information	
Timeframe for reporting adverse events: End of trial at 8 weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21
Reporting groups	
Reporting group title	Active treatment
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Active treatment	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (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: 1 %

Non-serious adverse events	Active treatment	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 50 (46.00%)	22 / 52 (42.31%)	
Gastrointestinal disorders			
Pain	Additional description: Abdominal pain was reported in 21.5% of the misoprostol group vs 24.6% of the placebo group		
subjects affected / exposed	10 / 50 (20.00%)	13 / 52 (25.00%)	
occurrences (all)	10	13	
Diarrhoea	Additional description: Diarrhoea was reported by 20% of the misoprostol group vs. 14% of the placebo group		
subjects affected / exposed	11 / 50 (22.00%)	6 / 52 (11.54%)	
occurrences (all)	11	6	
Vomiting	Additional description: Nausea/ vomiting were reported by 20% of the misoprostol group vs 19.3% of the placebo group		
subjects affected / exposed	9 / 50 (18.00%)	7 / 52 (13.46%)	
occurrences (all)	9	7	

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

N/A

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29754836