Clinical trial results:
A randomised placebo controlled trial of follow on Rifaximin for the prevention of relapse of Clostridium difficile associated diarrhoea.

Summary

EudraCT number	2012-003205-10
Trial protocol	GB
Global end of trial date	14 July 2016

Results information

Result version number	v3 (current)
This version publication date	22 September 2019
First version publication date	31 December 2018
Version creation reason	• Correction of full data set Correction of dates in results analysis stage section Correction of p-value for primary analysis. Correction of adverse event data. Addition of protocol amendment information
Summary attachment (see zip file)	RAPID trial published in Gut (Major, 2018 RAPID trial full paper gutjnl-2018-316794.full.pdf)

Trial information

Trial identification

Sponsor protocol code	12072

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Nottingham
Sponsor organisation address	Kingsmeadow campus, Nottingham, United Kingdom, NG7 2NR
Public contact	Spiller, University of Nottingham, 44 01158231090, robin.spiller@nottingham.ac.uk
Scientific contact	Spiller, University of Nottingham, 44 01158231090, 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 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	23 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 July 2016
Global end of trial reached?	Yes
Global end of trial date	14 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To look at whether a course of Rifaximin after a patient has been successfully treated for C.difficile diarrhoeal infection with a standard course of antibiotics can reduce the rate of the infection returning (recurrence)

Protection of trial subjects:

Usual measures Very safe drug so risk small

Background therapy:

None

Evidence for comparator:

Placebo controlled as unclear if intervention was beneficial

Actual start date of recruitment	11 December 2012
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: 151
Worldwide total number of subjects	151
EEA total number of subjects	151

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)	41
From 65 to 84 years	80
85 years and over	30

Subject disposition

Recruitment

Recruitment details:

Participants were recruited between 11 December 2012 and 7 March 2016. Those eligible for inclusion (see online supplementary file 1) were adults aged 18 years or older with a confirmed case of CDI that was successfully treated with metronidazole or vancomycin. This included primary, recurrent and multiply recurrent CDI episodes.

Pre-assignment

Screening details:

Participants were recruited between 11 December 2012 and 7 March 2016. Those eligible for inclusion (see online supplementary file 1) were adults aged 18 years or older with a confirmed case of CDI that was successfully treated with metronidazole or vancomycin. This included primary, recurrent and multiply recurrent CDI episodes.

Pre-assignment period milestones

Number of subjects started	2157[1]
Number of subjects completed	151

Pre-assignment subject non-completion reasons

Reason: Number of subjects	did not meet eligibility: 736
Reason: Number of subjects	declined to participate: 460
Reason: Number of subjects	other: 443
Reason: Number of subjects	consent unobtainable: 138
Reason: Number of subjects	unable to contact: 136
Reason: Number of subjects	unknown: 93

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 2157 were screened but only 151 were randomised

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

Blinding implementation details:

Participants were given 126 tablets, containing either rifaximin 200 mg or an identical placebo formulation.

Arms

Are arms mutually exclusive?	Yes

Arm title	Placebo

Arm description:

Identical tablets to active

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

Dosage and administration details:

2 tablets t.d.s. for 2 weeks then 1 tablet t.d.s. for 2 weeks

Arm title	Active

Arm description:

The intended treatment regime was two tablets (400 mg rifaximin)
taken three times a day for 14 days, reduced to one tablet
(200 mg) three times a day for a further 14 days.

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

Dosage and administration details:

two tablets (400 mg rifaximin)
taken three times a day for 14 days, reduced to one tablet
(200 mg) three times a day for a further 14 days.

Number of subjects in period 1	Placebo	Active
Started	74	77
Completed	61	69
Not completed	13	8
Consent withdrawn by subject	8	7
death	5	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Identical tablets to active	
Reporting group title	Active
Reporting group description:	
The intended treatment regime was two tablets (400 mg rifaximin) taken three times a day for 14 days, reduced to one tablet (200 mg) three times a day for a further 14 days.	

Reporting group values	Placebo	Active	Total
Number of subjects	74	77	151
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	19	22	41
From 65-84 years	45	35	80
85 years and over	10	20	30
Age continuous Units: years			
arithmetic mean	71.5	72.2	
standard deviation	± 14.8	± 15.8	-
Gender categorical Units: Subjects			
Female	45	39	84
Male	29	38	67

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Identical tablets to active	
Reporting group title	Active
Reporting group description:	
The intended treatment regime was two tablets (400 mg rifaximin) taken three times a day for 14 days, reduced to one tablet (200 mg) three times a day for a further 14 days.	

Primary: CDI recurrence within 12 weeks of randomisation.

End point title	CDI recurrence within 12 weeks of randomisation.
End point description:	
The primary outcome was CDI recurrence within 12 weeks of randomisation. A recurrence was defined as three or more loose stools for two or more days in conjunction with a positive stool toxin assay. The primary outcome was determined by research nurses in each site confirming stool frequency with the study subject by direct questioning, together with the laboratory results.	
End point type	Primary
End point timeframe:	
12 weeks	

End point values	Placebo	Active		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61[1]	69		
Units: number of patients in whom CDI recurred				
CDI recurrence within 12 weeks	18	11		

Notes:

[1] - 8 withdrew 5 died

Statistical analyses

Statistical analysis title	Primary analysis
Statistical analysis description:	
All analyses were conducted according to allocated group (placebo or rifaximin) regardless of the amount of tablets actually taken. The primary analysis estimated the difference in percentage CDI recurrence between rifaximin and placebo groups at 12 weeks without imputation of missing outcome data. A generalised estimating equation was used with binomial family, identity link and an exchangeable correlation matrix to account for randomisation being stratified by hospital.	
Comparison groups	Placebo v Active

Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.06
Method	Generalised Estimating Equations
Parameter estimate	Risk difference (RD)
Point estimate	-13.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.1
upper limit	0.7

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events reported up to 6 month visit
Non serious adverse events reported up to week 8 visit

Adverse event reporting additional description:

In the results paper in Gut (2018, http:// dx.doi.org/10. 1136/gutjnl-2018-316794), SAEs and AEs were reported according to date of onset: starting up to 28 days post-randomisation (ie, during the treatment period) and starting 29 days or more after randomisation.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15/17.1

Reporting groups

Reporting group title	placebo

Reporting group description:

Participants taking at least one dose

Reporting group title	rifaximin

Reporting group description:

Participants taking at least one dose

Serious adverse events	placebo	rifaximin	
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 68 (47.06%)	32 / 73 (43.84%)	
number of deaths (all causes)	7	9	
number of deaths resulting from adverse events	7	9	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Prepuce dorsal slit			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Stent placement			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric calculus removal			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 68 (0.00%)	3 / 73 (4.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adverse drug reaction			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Death			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyrexia			
subjects affected / exposed	2 / 68 (2.94%)	2 / 73 (2.74%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suprapubic pain			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 68 (2.94%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 68 (1.47%)	2 / 73 (2.74%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 68 (4.41%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			

subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract stoma complication			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure congestive			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dementia Alzheimer's type			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 68 (1.47%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ascites			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intestinal perforation			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Megacolon			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal fibrosis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Alcoholic liver disease			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic hepatic failure			

subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	2 / 68 (2.94%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal injury			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 68 (1.47%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diverticulitis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cellulitis			
subjects affected / exposed	0 / 68 (0.00%)	2 / 73 (2.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	5 / 68 (7.35%)	3 / 73 (4.11%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	4 / 68 (5.88%)	7 / 73 (9.59%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 68 (2.94%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			

subjects affected / exposed	1 / 68 (1.47%)	2 / 73 (2.74%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sepsis			
subjects affected / exposed	2 / 68 (2.94%)	2 / 73 (2.74%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Septic shock			
subjects affected / exposed	0 / 68 (0.00%)	1 / 73 (1.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary tract infection			
subjects affected / exposed	1 / 68 (1.47%)	2 / 73 (2.74%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary tract infection fungal			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 68 (1.47%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	placebo	rifaximin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 68 (13.24%)	8 / 73 (10.96%)	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 68 (8.82%)	3 / 73 (4.11%)	
occurrences (all)	7	5	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	4 / 68 (5.88%)	5 / 73 (6.85%)	
occurrences (all)	4	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 August 2013	The diaries, blood and stool sampling were made optional; and the protocol, PIS and CFs amended to reflect this. Some of the secondary endpoints and eligibility criteria re-worded to reflect this or to provide clarification.
13 January 2015	Removal of the exclusion criterion: '5) unable to stop chronic antibiotic use'. Update so that Patient Invite Letter could be sent directly to community patients testing positive for C. difficile (previously through GP practices). Notification of extension of trial to September 2016.
02 October 2015	Addition of the exclusion criterion: '8) Taking ciclosporin' Introduction of voucher payments to participants in recognition of their contribution to the trial.

Notes:

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.

did not achieve intended recruitment numbers which were 180

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30254135