Clinical trial results:
Use of drug therapy in the management of symptomatic ureteric stones in hospitalised adults: a multicentre placebo controlled randomised trial of a calcium channel blocker(nifedipine)and an alpha blocker (tamsulosin) - The SUSPEND trial

Summary

EudraCT number	2010-019469-26
Trial protocol	GB
Global end of trial date	24 April 2014

Results information

Result version number	v1 (current)
This version publication date	12 May 2018
First version publication date	12 May 2018

Trial information

Trial identification

Sponsor protocol code	pRGF/016/09

Additional study identifiers

ISRCTN number	ISRCTN69423238
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	NHS Grampian
Sponsor organisation address	Foresterhill House Annex, Foresterhill,, Aberdeen, United Kingdom, AB25 2ZD
Public contact	Professor Sam McClinton, NHS Grampian, smcclinton@abdn.ac.uk
Scientific contact	Professor Sam McClinton, NHS Grampian, smcclinton@abdn.ac.uk
Sponsor organisation name	University of Aberdeen
Sponsor organisation address	Research Governance, Foresterhill House Annex,, Aberdeen, United Kingdom, AB25 2ZD
Public contact	Professor Sam McClinton, University of Aberdeen, smcclinton@nhs.net
Scientific contact	Professor Sam McClinton, University of Aberdeen, smcclinton@nhs.net

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	14 October 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 April 2014
Global end of trial reached?	Yes
Global end of trial date	24 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the project is to determine the clinical effectiveness and cost-effectiveness of the use of an alpha blocker(tamsulosin) and a calcium channel blocker (nifedipine) in the management of symptomatic urinary stones.

Protection of trial subjects:

Fully informed consent. Oversight by Sponsor, Data Monitoring Committee and Trial Steering Committee who reviewed accruing data.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 January 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: 1167
Worldwide total number of subjects	1167
EEA total number of subjects	1167

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)	1154
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Clinicians assessed patients presenting with suspected ureteric calculi against the eligibility criteria in accordance with standard practice. Eligible patients were approached and given a Patient Information Leaflet and given the opportunity to fully discuss the trial. All participants gave written consent.

Pre-assignment

Screening details:

Patients were identified by clinicians working in the urology or accident and emergency departments of participating sites, who were supported by local clinical research teams. Approved trial publicity material in he form of posters was used to help alert staff that the trial was taking place at specific sites.

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:

At randomisation, the participant was allocated a unique participant study number and assigned a numbered participant pack. The packs were provided by an independent supplier containing the over-encapsulated trial medication to ensure that the participant, local investigator and trial personnel remained blinded to treatment allocation.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Over-encapsulated lactose capsule

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:

Lactose capsule, once daily

Arm title	Tamsulosin Hydrochloride

Arm description:

Over-encapsulated capsule containing 400 ug tamsulosin (modified release)

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

Dosage and administration details:

400 ug, once daily up to 28 days

Arm title	Nifedipine

Arm description:

Over-encapsulated nifedipine (30 mg MR capsule)

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

Dosage and administration details:

Nifedipine, 30mg, once daily

Number of subjects in period 1[1]	Placebo	Tamsulosin Hydrochloride	Nifedipine
Started	384	383	383
Completed	379	378	379
Not completed	5	5	4
Lost to follow-up	5	5	4

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Number of subjects enrolled includes those later identified as post-randomisation exclusions. Number of subjects in the baseline period is the number enrolled minus those post-randomisation exclusions.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Over-encapsulated lactose capsule	
Reporting group title	Tamsulosin Hydrochloride
Reporting group description:	
Over-encapsulated capsule containing 400 ug tamsulosin (modified release)	
Reporting group title	Nifedipine
Reporting group description:	
Over-encapsulated nifedipine (30 mg MR capsule)	

Reporting group values	Placebo	Tamsulosin Hydrochloride	Nifedipine
Number of subjects	384	383	383
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	42.8	43.1	42.3
standard deviation	± 12.3	± 11.5	± 11.0
Gender categorical Units: Subjects			
Female	85	68	66
Male	299	315	317

Reporting group values	Total		
Number of subjects	1150		
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			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	219		
Male	931		

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description: Over-encapsulated lactose capsule	
Reporting group title	Tamsulosin Hydrochloride
Reporting group description: Over-encapsulated capsule containing 400 ug tamsulosin (modified release)	
Reporting group title	Nifedipine
Reporting group description: Over-encapsulated nifedipine (30 mg MR capsule)	

Primary: Primary outcome - no further intervention	
End point title	Primary outcome - no further intervention
End point description:	
End point type	Primary
End point timeframe: Four weeks	

End point values	Placebo	Tamsulosin Hydrochloride	Nifedipine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	379	378	379	
Units: Number participants				
number (not applicable)	303	307	304	

Statistical analyses

Statistical analysis title	Primary Outcome
Statistical analysis description: MET (Tamsulosin & Nifedipine) vs Placebo	
Comparison groups	Tamsulosin Hydrochloride v Nifedipine v Placebo
Number of subjects included in analysis	1136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.43

Statistical analysis title	Primary outcome
Statistical analysis description: Tamsulosin vs. Nifedipine	
Comparison groups	Tamsulosin Hydrochloride v Nifedipine
Number of subjects included in analysis	757
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.53

Statistical analysis title	Primary outcome
Statistical analysis description: Tamsulosin vs. placebo	
Comparison groups	Placebo v Tamsulosin Hydrochloride
Number of subjects included in analysis	757
Analysis specification	Post-hoc
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.78

Statistical analysis title	Primary Outcome
Comparison groups	Nifedipine v Placebo

Number of subjects included in analysis	758
Analysis specification	Post-hoc
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.56

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Sixteen weeks	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	None
Dictionary version	0

Reporting groups	
Reporting group title	Nifedipine
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Tamsulosin
Reporting group description: -	

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: Non-serious adverse events were not collected for the study as both IMPs were established, marketed products with a known safety profile

Serious adverse events	Nifedipine	Placebo	Tamsulosin
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 383 (3.13%)	6 / 384 (1.56%)	9 / 383 (2.35%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 383 (0.00%)	0 / 384 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Chest pain			
subjects affected / exposed	2 / 383 (0.52%)	0 / 384 (0.00%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 383 (0.26%)	0 / 384 (0.00%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Crohn's disease			
subjects affected / exposed	0 / 383 (0.00%)	0 / 384 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 383 (0.00%)	0 / 384 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Shortness of breath			
subjects affected / exposed	1 / 383 (0.26%)	0 / 384 (0.00%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Right loin pain			
subjects affected / exposed	1 / 383 (0.26%)	0 / 384 (0.00%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	8 / 383 (2.09%)	4 / 384 (1.04%)	6 / 383 (1.57%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 383 (0.00%)	1 / 384 (0.26%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Nifedipine	Placebo	Tamsulosin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 383 (0.00%)	0 / 384 (0.00%)	0 / 383 (0.00%)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 May 2011	During the initial stages of the trial, a number of SAEs were reported and recorded which, on investigation, were found to be a result of readmissions for continuing treatment of the participant's ureteric stone (i.e. the primary outcome). These were, therefore, being recorded as a SAE as well as an outcome. To ensure that such events were recorded only as an outcome, the wording regarding the collection of these events was clarified to state: Hospital admissions (planned or unplanned) associated with the treatment of the ureteric stone diagnosed at the time of entry to the trial are expected. These will be recorded as an outcome measure, but will not be recorded or reported as serious adverse events.

Notes:

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/26244520

http://www.ncbi.nlm.nih.gov/pubmed/25998582