Clinical trial results:
Onabotulinum toxin-A versus extended release tolterodine in the management of idiopathic overactive bladder in children: A pilot randomised controlled trial (OVERT)

Summary

EudraCT number	2014-001068-36
Trial protocol	GB
Global end of trial date	06 March 2018

Results information

Result version number	v1 (current)
This version publication date	13 March 2019
First version publication date	13 March 2019

Trial information

Trial identification

Sponsor protocol code	R03465

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	RfPB: PB-PG-0712-28094

Notes:

Sponsors

Sponsor organisation name	Manchester University NHS Foundation Trust
Sponsor organisation address	1st Floor Nowgen Building, 29 Grafton Street, Manchester, United Kingdom, M13 9WU
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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	06 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 June 2017
Global end of trial reached?	Yes
Global end of trial date	06 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principle objective of the pilot study is to ensure that a full randomised control trial (RCT) is logistically feasible and acceptable to patients.

We will collect the following information to allow us to plan the main trial:

1. Eligibility rate of the patients screened - how many meet the eligibility criteria.

2. Recruitment rate of the eligible patients - how many consent to take part in the study.

3. Acceptability of randomisation to those patients consenting - how many are actually randomised, and of those randomised how many receive the treatment allocated.

4. Primary outcome data for the power calculation.

5. Loss to follow up rate of the patients randomised how many children will continue to be willing to participate throughout the study

6. Acceptability and suitability of urodynamic studies to assess secondary outcome measures

Protection of trial subjects:

A urodynamic study will be done as part of baseline assessment. This is a routine practice in patients who are not responding to standard medical treatment as is the case with our participants. Urodynamic study requires a general anaesthetic as a standard procedure. Parental feelings were explored at the focus group meeting and in the questionnaire with regard to the requirement for a general anaesthetic. While this is of some concern they accept that this is necessary.

The study design requires a urodynamic study under general anaesthetic at 6 weeks after initiation of treatment which is not always performed in routine clinical practice. The urodynamic study is felt to be necessary to assess the response to treatment in an objective way. Parental feelings were explored at the focus group meeting and in the questionnaire with regard to the requirement for a second general anaesthetic and urodynamic study. Parents and patients with experience of having a urodynamic study reported minimal concerns. Parents accepted that urodynamic data was required to objectively measure any improvement in bladder function.

The study group considered all options before formulating the current research plan. While a double blind randomised study is ideal, in our view performing a blinded study comparing onaBtA with placebo injections at cystoscopy would be unethical considering the general anaesthetic involved. Hence we are proposing this as a non blinded study comparing onaBtA with extended release tolterodine.

Extended release tolterodine is dispensed as a capsule. Younger children may not be able to swallow a capsule. We have checked with the pharmacist and the capsules can be opened and granules can be taken with fluid/yoghurt/jelly making it feasible for all age groups to have the medication.

Background therapy:

none

Evidence for comparator:

The decision to compare the effectiveness of Botox® with Tolterodine XL (extended release tolterodine)

was taken, as most patients would either have not been commenced on Tolterodine XL or may have had tolterodine at a lower dose. However there would be a tiny proportion that may have had Tolterodine XL at 4mg dose. A 4mg dose would be applicable to all children in the study group and in children who cannot swallow a capsule it is possible to open the capsule without affecting the pharmacokinetics (2010, The NEWT Guidelines for Administration of Medication to Patients with Enteral Feeding Tubes or Swallowing Difficulties).

Actual start date of recruitment	11 February 2015
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: 46
Worldwide total number of subjects	46
EEA total number of subjects	46

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)	35
Adolescents (12-17 years)	11
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment took place at Manchester Royal Infirmary. PIC sites were added in an amendment however this came in too late to have an impact as only one patient was recruited through the PICs. Recruitment to screening phase began in February 2015 and the first patient was randomised in August 2015; 46 patients were randomised in total.

Pre-assignment

Screening details:

There were a total of 98 patients assessed for eligibility. Eighty-five patients (87%) were eligible to proceed to the screening phase and the parents of 62 of these patients (73%) were willing to provide consent. Forty-six patients remained eligible at the end of the screening stage (74%) and went on to be randomised.

Period 1

Period 1 title	Full trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Tolterodine

Arm description:

Extended-release Tolterodine XL 4mg orally

Arm type	Active comparator
Investigational medicinal product name	Tolterodine XL
Investigational medicinal product code	
Other name	Tolterodine, Extended-release Tolterodine
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

4mg extended-release Tolterodine XL to be taken once daily via oral administration for the duration of the trial

Arm title	Botox

Arm description:

Single administration of Onabotulinum Toxin A (onaBtA; 5 IU/Kg, maximum 150 IU) into the bladder

Arm type	Experimental
Investigational medicinal product name	Onabotulinum toxin A
Investigational medicinal product code	
Other name	Botox
Pharmaceutical forms	Injection
Routes of administration	Intravesical use

Dosage and administration details:

A single dose of 5 IU/kg up to a maximum of 150 IU constituted in 0.9% saline to a dilution of 10 IU per ml. Under general anaesthetic multiple injections are given intravesically in the submucosal layer of the bladder. A trigone sparing technique under the guidance of rigid cystoscopy is used.

Number of subjects in period 1	Tolterodine	Botox
Started	24	22
Completed	24	20
Not completed	0	2
Lost to follow-up	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Tolterodine
Reporting group description:	
Extended-release Tolterodine XL 4mg orally	
Reporting group title	Botox
Reporting group description:	
Single administration of Onabotulinum Toxin A (onaBtA; 5 IU/Kg, maximum 150 IU) into the bladder	

Reporting group values	Tolterodine	Botox	Total
Number of subjects	24	22	46
Age categorical Units: Subjects			
Children (2-11 years)	17	18	35
Adolescents (12-17 years)	7	4	11
Age continuous Units: years			
arithmetic mean	10.2	10.2	
standard deviation	± 2.6	± 2.1	-
Gender categorical Units: Subjects			
Female	16	13	29
Male	8	9	17
Previous bladder training Units: Subjects			
Yes	22	21	43
No	2	1	3
Urinalysis Units: Subjects			
Normal	18	18	36
Abnormal	6	4	10
Urodynamic study: presence of detrusor overactivity Units: Subjects			
Yes	21	19	40
No	3	3	6
Prescribed prophylactic antibiotics Units: Subjects			
Yes	23	22	45
No	1	0	1
Overall assessment: reduced capacity Units: Subjects			
Yes	17	14	31
No	7	8	15
Overall assessment: reduced compliance Units: Subjects			
Yes	11	10	21

No	13	12	25
Overall assessment: presence of detrusor overactivity Units: Subjects			
Yes	21	19	40
No	3	3	6
SAQ: did nocturnal enuresis occur? Units: Subjects			
Yes	19	15	34
No	3	2	5
Missing	2	5	7
Height Units: cm			
arithmetic mean	136.4	138.1	
standard deviation	± 15.3	± 12.9	-
Weight Units: kg			
arithmetic mean	35.7	36.9	
standard deviation	± 15.8	± 17.2	-
Uroflowmetry 1: maximum voided volume Units: ml			
arithmetic mean	147.9	130.2	
standard deviation	± 95.0	± 70.1	-
Uroflowmetry 1: post-void residual volume Units: ml			
arithmetic mean	21.5	23.7	
standard deviation	± 27.8	± 26.0	-
Uroflowmetry 2: maximum voided volume Units: ml			
arithmetic mean	156.9	146.0	
standard deviation	± 105.4	± 109.0	-
Uroflowmetry 2: post-void residual volume Units: ml			
arithmetic mean	34.5	15.9	
standard deviation	± 39.0	± 22.8	-
Uroflowmetry 3: maximum voided volume Units: ml			
arithmetic mean	165.2	110.3	
standard deviation	± 104.6	± 76.5	-
Uroflowmetry 3: post-void residual volume Units: ml			
arithmetic mean	13.5	8.5	
standard deviation	± 24.4	± 15.0	-
Urodynamic study: maximum cystometric capacity Units: ml			
arithmetic mean	218.0	246.2	
standard deviation	± 104.0	± 105.8	-

Urodynamic study: maximum detrusor pressure during detrusor overactivity			
Units: cm of water			
arithmetic mean	53.4	35.1	
standard deviation	± 43.5	± 16.5	-
Urodynamic study: number of overactive contractions			
Units: contractions			
arithmetic mean	6.2	7.3	
standard deviation	± 3.7	± 5.5	-
Urodynamic study: maximum detrusor pressure during storage phase			
Units: cm of water			
arithmetic mean	14.9	17.1	
standard deviation	± 7.5	± 11.1	-
Urodynamic study: bladder compliance			
Units: ml/cm water			
arithmetic mean	21.6	19.6	
standard deviation	± 20.8	± 15.6	-
Urodynamic study: post-void residual urine			
Units: ml			
arithmetic mean	7.0	10.0	
standard deviation	± 17.7	± 22.4	-
SAQ: number of wetting episodes per day			
Units: wetting episodes per day			
arithmetic mean	2.6	2.7	
standard deviation	± 1.3	± 2.0	-
SAQ: number of wees per day			
Units: wees per day			
arithmetic mean	8.4	7.6	
standard deviation	± 2.8	± 1.6	-
SAQ: number of episodes of urinary urgency per day			
Units: episodes per day			
arithmetic mean	4.2	3.7	
standard deviation	± 2.0	± 1.9	-
SAQ: number of episodes of nocturia per day			
Units: episodes per day			
arithmetic mean	0.6	0.4	
standard deviation	± 0.8	± 0.7	-

End points

End points reporting groups

Reporting group title	Tolterodine
Reporting group description:	
Extended-release Tolterodine XL 4mg orally	
Reporting group title	Botox
Reporting group description:	
Single administration of Onabotulinum Toxin A (onaBtA; 5 IU/Kg, maximum 150 IU) into the bladder	

Primary: Six-week SAQ: number of wetting episodes per day

End point title	Six-week SAQ: number of wetting episodes per day[1]
End point description:	
End point type	Primary
End point timeframe:	
Week 6 post-randomisation	

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: Pilot trial - descriptive statistics only

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	15		
Units: episodes per day				
arithmetic mean (standard deviation)	1.6 (± 1.0)	1.4 (± 1.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week urodynamic study: maximum cystometric capacity

End point title	Six-week urodynamic study: maximum cystometric capacity
End point description:	
End point type	Secondary
End point timeframe:	
Week 6 post-randomisation	

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	17		
Units: ml				
arithmetic mean (standard deviation)	252.9 (± 97.7)	336.4 (± 166.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week urodynamic study: detrusor overactivity

End point title	Six-week urodynamic study: detrusor overactivity

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	17		
Units: patients				
Present	16	8		
Absent	2	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week urodynamic study: maximum detrusor pressure during storage phase

End point title	Six-week urodynamic study: maximum detrusor pressure during storage phase

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	17		
Units: cm of water				
arithmetic mean (standard deviation)	15.3 (± 11.4)	16.2 (± 8.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week urodynamic study: bladder compliance

End point title	Six-week urodynamic study: bladder compliance

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	17		
Units: ml/cm water				
arithmetic mean (standard deviation)	26.9 (± 40.8)	28.9 (± 25.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week urodynamic study: post-void residual urine

End point title	Six-week urodynamic study: post-void residual urine

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	17		
Units: ml				
arithmetic mean (standard deviation)	16.6 (± 23.8)	61.2 (± 54.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month SAQ: number of wetting episodes per day

End point title	Three-month SAQ: number of wetting episodes per day

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	13		
Units: episodes per day				
arithmetic mean (standard deviation)	1.5 (± 1.1)	1.9 (± 1.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month SAQ: number of wetting episodes per day

End point title	Six-month SAQ: number of wetting episodes per day

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	10		
Units: episodes per day				
arithmetic mean (standard deviation)	1.0 (± 0.6)	2.0 (± 1.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week SAQ: number of wees per day

End point title	Six-week SAQ: number of wees per day

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	19		
Units: wees per day				
arithmetic mean (standard deviation)	7.2 (± 2.1)	6.7 (± 1.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month SAQ: number of wees per day

End point title	Three-month SAQ: number of wees per day

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	16		
Units: wees per day				
arithmetic mean (standard deviation)	7.7 (± 3.2)	6.8 (± 1.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month SAQ: number of wees per day

End point title	Six-month SAQ: number of wees per day

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	13		
Units: wees per day				
arithmetic mean (standard deviation)	7.1 (± 2.1)	7.8 (± 1.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week SAQ: number of episodes of urinary urgency per day

End point title	Six-week SAQ: number of episodes of urinary urgency per day

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	19		
Units: episodes per day				
arithmetic mean (standard deviation)	3.2 (± 2.0)	2.8 (± 1.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month SAQ: number of episodes of urinary urgency per day

End point title	Three-month SAQ: number of episodes of urinary urgency per day

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	14		
Units: episodes per day				
arithmetic mean (standard deviation)	3.5 (± 2.4)	2.7 (± 1.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month SAQ: number of episodes of urinary urgency per day

End point title	Six-month SAQ: number of episodes of urinary urgency per day

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	12		
Units: episodes per day				
arithmetic mean (standard deviation)	2.4 (± 1.6)	3.2 (± 2.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week SAQ: number of episodes of nocturia per day

End point title	Six-week SAQ: number of episodes of nocturia per day

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	15		
Units: episodes per day				
arithmetic mean (standard deviation)	0.5 (± 0.5)	0.5 (± 0.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month SAQ: number of episodes of nocturia per day

End point title	Three-month SAQ: number of episodes of nocturia per day

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	13		
Units: episodes per day				
arithmetic mean (standard deviation)	0.7 (± 0.7)	0.6 (± 0.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month SAQ: number of episodes of nocturia per day

End point title	Six-month SAQ: number of episodes of nocturia per day

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	11		
Units: episodes per day				
arithmetic mean (standard deviation)	0.6 (± 0.7)	0.7 (± 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week SAQ: did nocturnal enuresis occur?

End point title	Six-week SAQ: did nocturnal enuresis occur?

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17		
Units: patients				
Yes	19	13		
No	3	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month SAQ: did nocturnal enuresis occur?

End point title	Three-month SAQ: did nocturnal enuresis occur?

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	15		
Units: patients				
Yes	16	11		
No	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month SAQ: did nocturnal enuresis occur?

End point title	Six-month SAQ: did nocturnal enuresis occur?

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	12		
Units: patients				
Yes	14	9		
No	4	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month bladder capacity

End point title	Three-month bladder capacity

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	18		
Units: ml				
arithmetic mean (standard deviation)	211.7 (± 138.0)	208.8 (± 106.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month bladder capacity

End point title	Six-month bladder capacity

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	16		
Units: ml				
arithmetic mean (standard deviation)	225.4 (± 118.1)	230.4 (± 100.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month post-void residual urine

End point title	Three-month post-void residual urine

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	18		
Units: ml				
arithmetic mean (standard deviation)	18.2 (± 23.3)	27.3 (± 27.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month post-void residual urine

End point title	Six-month post-void residual urine

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	16		
Units: ml				
arithmetic mean (standard deviation)	42.0 (± 33.0)	19.4 (± 24.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week PedsQL: Physical functioning (parent report)

End point title	Six-week PedsQL: Physical functioning (parent report)

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: score				
arithmetic mean (standard deviation)	91.1 (± 8.0)	77.1 (± 20.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week PedsQL: Physical functioning (patient report)

End point title	Six-week PedsQL: Physical functioning (patient report)

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	13		
Units: score				
arithmetic mean (standard deviation)	80.5 (± 17.5)	87.7 (± 12.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month PedsQL: Physical functioning (parent report)

End point title	Three-month PedsQL: Physical functioning (parent report)

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	3		
Units: score				
arithmetic mean (standard deviation)	70.0 (± 33.7)	89.6 (± 4.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month PedsQL: Physical functioning (patient report)

End point title	Three-month PedsQL: Physical functioning (patient report)

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	13		
Units: score				
arithmetic mean (standard deviation)	79.1 (± 23.9)	80.5 (± 19.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month PedsQL: Physical functioning (parent report)

End point title	Six-month PedsQL: Physical functioning (parent report)

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: score				
arithmetic mean (standard deviation)	80.2 (± 34.3)	78.1 (± 13.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month PedsQL: Physical functioning (patient report)

End point title	Six-month PedsQL: Physical functioning (patient report)

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	13		
Units: score				
arithmetic mean (standard deviation)	79.5 (± 19.4)	83.7 (± 19.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week PedsQL: Emotional functioning (parent report)

End point title	Six-week PedsQL: Emotional functioning (parent report)

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: score				
arithmetic mean (standard deviation)	63.6 (± 20.6)	60.0 (± 23.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week PedsQL: Emotional functioning (patient report)

End point title	Six-week PedsQL: Emotional functioning (patient report)

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	13		
Units: score				
arithmetic mean (standard deviation)	69.7 (± 28.6)	70.0 (± 30.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month PedsQL: Emotional functioning (parent report)

End point title	Three-month PedsQL: Emotional functioning (parent report)

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	3		
Units: score				
arithmetic mean (standard deviation)	59.0 (± 35.2)	45.0 (± 39.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month PedsQL: Emotional functioning (patient report)

End point title	Three-month PedsQL: Emotional functioning (patient report)

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	13		
Units: score				
arithmetic mean (standard deviation)	74.0 (± 23.5)	61.5 (± 31.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month PedsQL: Emotional functioning (parent report)

End point title	Six-month PedsQL: Emotional functioning (parent report)

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: score				
arithmetic mean (standard deviation)	75.0 (± 43.3)	45.0 (± 49.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month PedsQL: Emotional functioning (patient report)

End point title	Six-month PedsQL: Emotional functioning (patient report)

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	13		
Units: score				
arithmetic mean (standard deviation)	68.9 (± 24.5)	67.7 (± 25.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week PedsQL: Social functioning (parent report)

End point title	Six-week PedsQL: Social functioning (parent report)

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: score				
arithmetic mean (standard deviation)	78.6 (± 22.5)	50.0 (± 27.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week PedsQL: Social functioning (patient report)

End point title	Six-week PedsQL: Social functioning (patient report)

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	13		
Units: score				
arithmetic mean (standard deviation)	75.3 (± 22.3)	88.1 (± 17.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month PedsQL: Social functioning (parent report)

End point title	Three-month PedsQL: Social functioning (parent report)

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	3		
Units: score				
arithmetic mean (standard deviation)	75.0 (± 30.6)	41.7 (± 38.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month PedsQL: Social functioning (patient report)

End point title	Three-month PedsQL: Social functioning (patient report)

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	13		
Units: score				
arithmetic mean (standard deviation)	72.3 (± 30.5)	88.1 (± 19.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month PedsQL: Social functioning (parent report)

End point title	Six-month PedsQL: Social functioning (parent report)

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: score				
arithmetic mean (standard deviation)	91.7 (± 14.4)	37.5 (± 17.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month PedsQL: Social functioning (patient report)

End point title	Six-month PedsQL: Social functioning (patient report)

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	13		
Units: score				
arithmetic mean (standard deviation)	80.0 (± 28.9)	88.8 (± 14.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week PedsQL: School functioning (parent report)

End point title	Six-week PedsQL: School functioning (parent report)

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: score				
arithmetic mean (standard deviation)	68.6 (± 23.4)	50.0 (± 21.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week PedsQL: School functioning (patient report)

End point title	Six-week PedsQL: School functioning (patient report)

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	13		
Units: score				
arithmetic mean (standard deviation)	66.3 (± 21.3)	66.2 (± 22.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month PedsQL: School functioning (parent report)

End point title	Three-month PedsQL: School functioning (parent report)

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	3		
Units: score				
arithmetic mean (standard deviation)	60.0 (± 42.3)	65.0 (± 10.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month PedsQL: School functioning (patient report)

End point title	Three-month PedsQL: School functioning (patient report)

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	13		
Units: score				
arithmetic mean (standard deviation)	62.0 (± 30.5)	66.2 (± 25.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month PedsQL: School functioning (parent report)

End point title	Six-month PedsQL: School functioning (parent report)

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: score				
arithmetic mean (standard deviation)	71.7 (± 32.1)	65.0 (± 14.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month PedsQL: School functioning (patient report)

End point title	Six-month PedsQL: School functioning (patient report)

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	13		
Units: score				
arithmetic mean (standard deviation)	67.5 (± 23.0)	67.7 (± 23.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week PedsQL: Psychosocial health (parent report)

End point title	Six-week PedsQL: Psychosocial health (parent report)

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: score				
arithmetic mean (standard deviation)	70.2 (± 14.8)	53.3 (± 22.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week PedsQL: Psychosocial health (patient report)

End point title	Six-week PedsQL: Psychosocial health (patient report)

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	13		
Units: score				
arithmetic mean (standard deviation)	70.4 (± 21.4)	74.7 (± 20.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month PedsQL: Psychosocial health (parent report)

End point title	Three-month PedsQL: Psychosocial health (parent report)

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	3		
Units: score				
arithmetic mean (standard deviation)	64.7 (± 35.1)	50.6 (± 28.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month PedsQL: Psychosocial health (patient report)

End point title	Three-month PedsQL: Psychosocial health (patient report)

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	13		
Units: score				
arithmetic mean (standard deviation)	69.4 (± 26.3)	71.9 (± 22.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month PedsQL: Psychosocial health (parent report)

End point title	Six-month PedsQL: Psychosocial health (parent report)

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: score				
arithmetic mean (standard deviation)	79.4 (± 29.9)	49.2 (± 17.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month PedsQL: Psychosocial health (patient report)

End point title	Six-month PedsQL: Psychosocial health (patient report)

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	13		
Units: score				
arithmetic mean (standard deviation)	72.1 (± 21.5)	74.7 (± 18.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week PedsQL: Total score (parent report)

End point title	Six-week PedsQL: Total score (parent report)

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: score				
arithmetic mean (standard deviation)	75.3 (± 14.8)	61.6 (± 19.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week PedsQL: Total score (patient report)

End point title	Six-week PedsQL: Total score (patient report)

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	13		
Units: score				
arithmetic mean (standard deviation)	73.9 (± 18.0)	79.3 (± 15.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month PedsQL: Total score (parent report)

End point title	Three-month PedsQL: Total score (parent report)

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	3		
Units: score				
arithmetic mean (standard deviation)	66.5 (± 34.1)	64.1 (± 20.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month PedsQL: Total score (patient report)

End point title	Three-month PedsQL: Total score (patient report)

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	13		
Units: score				
arithmetic mean (standard deviation)	72.8 (± 24.2)	74.9 (± 20.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month PedsQL: Total score (parent report)

End point title	Six-month PedsQL: Total score (parent report)

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: score				
arithmetic mean (standard deviation)	79.7 (± 31.4)	59.2 (± 16.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month PedsQL: Total score (patient report)

End point title	Six-month PedsQL: Total score (patient report)

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	13		
Units: score				
arithmetic mean (standard deviation)	74.7 (± 19.5)	77.8 (± 17.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-week PinQ

End point title	Six-week PinQ

End point description:

End point type	Secondary

End point timeframe:

Week 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	16		
Units: score				
arithmetic mean (standard deviation)	1.7 (± 0.8)	1.6 (± 0.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Three-month PinQ

End point title	Three-month PinQ

End point description:

End point type	Secondary

End point timeframe:

Month 3 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	17		
Units: score				
arithmetic mean (standard deviation)	1.5 (± 0.8)	1.7 (± 1.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Six-month PinQ

End point title	Six-month PinQ

End point description:

End point type	Secondary

End point timeframe:

Month 6 post-randomisation

End point values	Tolterodine	Botox		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	15		
Units: score				
arithmetic mean (standard deviation)	1.5 (± 0.8)	1.5 (± 0.8)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Twenty-eight days from last dose or last trial follow-up	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21

Reporting groups	
Reporting group title	Tolterodine
Reporting group description:	
Extended-release Tolterodine XL 4mg orally	
Reporting group title	Botox
Reporting group description:	
Single administration of Onabotulinum Toxin A (onaBtA; 5 IU/Kg, maximum 150 IU) into the bladder	

Serious adverse events	Tolterodine	Botox	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Tolterodine	Botox	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 24 (37.50%)	8 / 22 (36.36%)	
Injury, poisoning and procedural complications			
Abdominal injury			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	1 / 24 (4.17%)	1 / 22 (4.55%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	1 / 24 (4.17%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	3 / 24 (12.50%)	1 / 22 (4.55%)	
occurrences (all)	4	1	
Anal incontinence			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	1 / 24 (4.17%)	1 / 22 (4.55%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Nausea			

subjects affected / exposed	1 / 24 (4.17%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	0 / 24 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Wheezing			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	2	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	3	
Infections and infestations			
Rhinitis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	4 / 24 (16.67%)	3 / 22 (13.64%)	
occurrences (all)	9	4	
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 June 2015	Protocol version 5.0 - Following Trial Steering Committee (TSC), Data monitoring committee (DMC), and trial management group (TMG) meetings there were elements of the protocol that were deemed to be ambiguous. Based on these conversations, clarifications were provided in the protocol and associated documents. The most substantial change is the clarification of the measurement of the primary outcome. The protocol was changed to detail a seven day symptom assessment questionnaire instead of a two day one as this was unclear. The protocol stated that the DMC would advise on interim analyses which the committee said was not possible so this was removed. The TMG discussed a number of more minor changes to the protocol which were implemented as well.
11 May 2016	Protocol version 6.0 - The main purpose of this amendment was to increase recruitment by the addition of patient identification centres. In addition the Children's Continence Service, Children's Community Services and Central Manchester University Hospitals NHS Foundation Trust (CMFT) will identify potential participants on behalf of the CMFT and if a potential participant is interested, we will request a clinical referral from the GP.
05 February 2018	Change of sponsor amendment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported