



## Clinical trial results:

**The effect of intravesical Lidocaine solution versus placebo as anesthesia prior to intravesical injection of onabotulinum toxin A. A randomized, double-blind, placebo controlled cross-over study**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2021-000559-38 |
| Trial protocol           | DK             |
| Global end of trial date | 10 May 2024    |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 13 May 2025  |
| First version publication date | 13 May 2025  |

### Trial information

#### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | BTXA2021 |
|-----------------------|----------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT05415865 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Herlev and Gentofte Hospital   |
| Sponsor organisation address | Borgmester Ib Juuls Vej 1, 16. etage, Herlev, Denmark, 2730  |
| Public contact               | Department of Obstetrics and Gynecology<br><br>, Herlev and Gentofte University Hospital, Department of Obstetrics and Gynecology, +45 38681406, niels.klarskov@regionh.dk |
| Scientific contact           | Department of Obstetrics and Gynecology<br>, Herlev and Gentofte University Hospital, Department of Obstetrics and Gynecology, +45 38681406, niels.klarskov@regionh.dk     |

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                       | 01 September 2024 |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 10 May 2024       |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the effect of intravesical alkalinised lidocaine as an anaesthetic treatment on procedural pain during intradetrusor onabotulinumtoxinA injections for overactive bladder.

Protection of trial subjects:

A follow up call one week was conducted, where patients were asked about adverse effects and experience with the treatment.

Background therapy:

Intradetrusor onabotulinumtoxinA injections

Evidence for comparator:

Alkalinized lidocaine was not previously compared to placebo (saline).

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 15 November 2022 |
| 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 | Denmark: 50 |
| Worldwide total number of subjects   | 50          |
| EEA total number of subjects         | 50          |

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)                      | 16 |
| From 65 to 84 years                       | 32 |
| 85 years and over                         | 2  |

## Subject disposition

### Recruitment

Recruitment details:

Women aged  $\geq 18$  years referred for treatment with onabotulinumtoxinA injections due to complaints of OAB symptoms. Patients should accept to receive BTX-A injections in an outpatient clinic without the option of sedation.

### Pre-assignment

Screening details:

60 women scheduled for BTX-A treatment between September 2022 and May 2023 were screened. Of these, 50 signed informed consent, met eligibility criteria and completed the first treatment period.

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | First onabotulinumtoxinA inj. in trial                        |
| 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:

All personnel involved in enrolment, randomisation, medication administration, and outcome assessment remained blinded until the outcomes were analysed.

### Arms

|                              |                       |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes                   |
| Arm title                    | Alkalinized lidocaine |

Arm description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period.

In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period

|  |                         |
|--|-------------------------|
| Arm type                               | Active comparator       |
| Investigational medicinal product name | Lidokain SAD            |
| Investigational medicinal product code |                         |
| Other name                             | LIDOCAINE HYDROCHLORIDE |
| Pharmaceutical forms                   | Injection               |
| Routes of administration               | Intravesical use        |

Dosage and administration details:

Lidocaine hydrochloride 20 mg/mL, 20 mL was mixed with sodium hydrogen carbonate 1 mmol/mL, 10 mL; and sodium chloride 9 g/L, 10 mL. The buffer was instilled in the bladder with a Luer lock catheter.

|  |                           |
|--|---------------------------|
| Investigational medicinal product name | Natriumbikarbonat SAD     |
| Investigational medicinal product code |                           |
| Other name                             | SODIUM HYDROGEN CARBONATE |
| Pharmaceutical forms                   | Injection                 |
| Routes of administration               | Intravesical use          |

Dosage and administration details:

Lidocaine hydrochloride 20 mg/mL, 20 mL was mixed with sodium hydrogen carbonate 1 mmol/mL, 10 mL; and sodium chloride 9 g/L, 10 mL. The buffer was instilled in the bladder with a Luer lock catheter.

|           |         |
|-----------|---------|
| Arm title | Placebo |
|-----------|---------|

Arm description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period. In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period

less

|  |                                 |
|--|---------------------------------|
| Arm type                               | Placebo                         |
| Investigational medicinal product name | Sodium chloride, NaCl SAD 9 g/l |
| Investigational medicinal product code |                                 |
| Other name                             |                                 |
| Pharmaceutical forms                   | Injection                       |
| Routes of administration               | Intravesical use                |

Dosage and administration details:

Sodium chloride 9 g/L, 20 mL; sodium chloride 9 g/L, 10 mL; and sodium chloride 9 g/L, 10 mL instilled in the bladder with Luer Lock catheter

| Number of subjects in period 1 | Alkalinized lidocaine | Placebo |
|--------------------------------|-----------------------|---------|
| Started                        | 25                    | 25      |
| Completed                      | 25                    | 25      |

## Period 2

|                              |   |
|------------------------------|---|
| Period 2 title               | Second onabotulinumtoxinA inj in trial                        |
| Is this the baseline period? | No  |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Blinding implementation details:

All personnel involved in enrolment, randomisation, medication administration, and outcome assessment remained blinded until the outcomes were analysed.

## Arms

|                              |                       |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes                   |
| Arm title                    | Alkalinized lidocaine |

Arm description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period.

In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period

|  |                         |
|--|-------------------------|
| Arm type                               | Active comparator       |
| Investigational medicinal product name | Lidokain SAD            |
| Investigational medicinal product code |                         |
| Other name                             | LIDOCAINE HYDROCHLORIDE |
| Pharmaceutical forms                   | Injection               |
| Routes of administration               | Intravesical use        |

Dosage and administration details:

Lidocaine hydrochloride 20 mg/mL, 20 mL was mixed with sodium hydrogen carbonate 1 mmol/mL, 10 mL; and sodium chloride 9 g/L, 10 mL. The buffer was instilled in the bladder with a Luer lock catheter.

|  |                           |
|--|---------------------------|
| Investigational medicinal product name | Natriumbikarbonat SAD     |
| Investigational medicinal product code |                           |
| Other name                             | SODIUM HYDROGEN CARBONATE |
| Pharmaceutical forms                   | Injection                 |
| Routes of administration               | Intravesical use          |

Dosage and administration details:

Lidocaine hydrochloride 20 mg/mL, 20 mL was mixed with sodium hydrogen carbonate 1 mmol/mL, 10 mL; and sodium chloride 9 g/L, 10 mL. The buffer was instilled in the bladder with a Luer lock catheter.

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

Arm description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period. In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period less

|  |                                 |
|--|---------------------------------|
| Arm type                               | Placebo                         |
| Investigational medicinal product name | Sodium chloride, NaCl SAD 9 g/l |
| Investigational medicinal product code |                                 |
| Other name                             |                                 |
| Pharmaceutical forms                   | Injection                       |
| Routes of administration               | Intravesical use                |

Dosage and administration details:

Sodium chloride 9 g/L, 20 mL; sodium chloride 9 g/L, 10 mL; and sodium chloride 9 g/L, 10 mL instilled in the bladder with Luer Lock catheter

| <b>Number of subjects in period 2</b> | Alkalinized lidocaine | Placebo |
|---------------------------------------|-----------------------|---------|
| Started                               | 25                    | 25      |
| Completed                             | 21                    | 20      |
| Not completed                         | 4                     | 5       |
| Consent withdrawn by subject          | -                     | 1       |
| Changed protocol                      | -                     | 2       |
| Received Myobloc                      | -                     | 1       |
| Changed protocol                      | 2                     | -       |
| Other healthcare issues               | 1                     | -       |
| Lost to follow-up                     | -                     | 1       |
| Protocol deviation                    | 1                     | -       |

## Baseline characteristics

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | First onabotulinumtoxinA inj. in trial |
|-----------------------|--|

Reporting group description: -

| Reporting group values                             | First onabotulinumtoxinA inj. in trial | Total |  |
|--|--|-------|--|
| Number of subjects                                 | 50                                     | 50    |  |
| Age categorical<br>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<br>Units: years                     |  |       |  |
| median   | 73                                     |       |  |
| inter-quartile range (Q1-Q3)                       | 63 to 78                               | -     |  |
| Gender categorical<br>Units: Subjects              |  |       |  |
| Female   | 50                                     | 50    |  |
| Male   | 0                                      | 0     |  |

## End points

### End points reporting groups

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Alkalinized lidocaine |
|-----------------------|-----------------------|

Reporting group description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period.

In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period. In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period less

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Alkalinized lidocaine |
|-----------------------|-----------------------|

Reporting group description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period.

In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period. In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period less

### Primary: Visual analogue scale (VAS) score

|                 |                                   |
|-----------------|-----------------------------------|
| End point title | Visual analogue scale (VAS) score |
|-----------------|-----------------------------------|

End point description:

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Maximum pain score reported using the 100-mm visual analogue scale (VAS) score immediately after BTX-A injections

| End point values                             | Alkalinized lidocaine | Placebo           | Alkalinized lidocaine | Placebo           |
|--|-----------------------|-------------------|-----------------------|-------------------|
| Subject group type                           | Reporting group       | Reporting group   | Reporting group       | Reporting group   |
| Number of subjects analysed                  | 25                    | 25                | 21                    | 20                |
| Units: millimetre(s)                         |                       |                   |                       |                   |
| least squares mean (confidence interval 95%) | 21.3 (14.7 to 27.8)   | 41.6 (35 to 48.1) | 21.3 (14.7 to 27.8)   | 41.6 (35 to 48.1) |

## Statistical analyses

|   |                                 |
|---|---------------------------------|
| <b>Statistical analysis title</b>   | ANCOVA                          |
| Statistical analysis description:<br>The difference in VAS pain scores between alkalinized lidocaine and placebo treatments was calculated using repeated measures analysis of covariance (ANCOVA ) |                                 |
| Comparison groups   | Alkalinized lidocaine v Placebo |
| Number of subjects included in analysis   | 45                              |
| Analysis specification  | Pre-specified                   |
| Analysis type   | other                           |
| P-value   | < 0.05                          |
| Method  | ANCOVA                          |
| Parameter estimate  | Mean difference (final values)  |
| Confidence interval   |                                 |
| level   | 95 %                            |
| sides   | 2-sided                         |
| Variability estimate  | Standard error of the mean      |

## Secondary: 5- point satisfaction score

|   |                             |
|---|-----------------------------|
| End point title   | 5- point satisfaction score |
| End point description:  |                             |
| End point type  | Secondary                   |
| End point timeframe:<br>One week after each BTX-A treatment, a follow-up call was scheduled asking the patients about their satisfaction with the BTX-A treatment using a 5-point Likert scale. |                             |

| End point values                  | Alkalinized lidocaine | Placebo         | Alkalinized lidocaine | Placebo         |
|-----------------------------------|-----------------------|-----------------|-----------------------|-----------------|
| Subject group type                | Reporting group       | Reporting group | Reporting group       | Reporting group |
| Number of subjects analysed       | 25                    | 25              | 21                    | 20              |
| Units: Ordinal                    |                       |                 |                       |                 |
| median (full range (min-max))     |                       |                 |                       |                 |
| 5- point satisfaction scale score | 5 (3 to 5)            | 5 (2 to 5)      | 5 (3 to 5)            | 5 (2 to 5)      |

## Statistical analyses



|  |                                  |
|--|----------------------------------|
| <b>Statistical analysis title</b>  | Wilcoxon signed-rank test        |
| Statistical analysis description:<br>Wilcoxon signed-rank test was used to compare 5-point satisfaction score. |                                  |
| Comparison groups  | Alkalinized lidocaine v Placebo  |
| Number of subjects included in analysis  | 45                               |
| Analysis specification   | Pre-specified                    |
| Analysis type  | other                            |
| P-value  | < 0.05                           |
| Method   | Wilcoxon (Mann-Whitney)          |
| Parameter estimate   | Median difference (final values) |
| Confidence interval  |                                  |
| level  | 95 %                             |
| sides  | 2-sided                          |
| Variability estimate   | Standard deviation               |

## Secondary: Urinary tract infection

|   |                         |
|---|-------------------------|
| End point title   | Urinary tract infection |
| End point description:  |                         |
| End point type  | Secondary               |
| End point timeframe:<br>Urinary tract infection (UTI) one week after each BTX-A treatment |                         |

| End point values            | Alkalinized lidocaine | Placebo         | Alkalinized lidocaine | Placebo         |
|-----------------------------|-----------------------|-----------------|-----------------------|-----------------|
| Subject group type          | Reporting group       | Reporting group | Reporting group       | Reporting group |
| Number of subjects analysed | 25                    | 25              | 21                    | 20              |
| Units: Number               | 5                     | 2               | 5                     | 2               |

## Statistical analyses

|  |                                 |
|--|---------------------------------|
| <b>Statistical analysis title</b>  | McNemars test                   |
| Statistical analysis description:<br>McNemars test was used to compare the UTI rate in intervention and placebo group. |                                 |
| Comparison groups  | Alkalinized lidocaine v Placebo |
| Number of subjects included in analysis  | 45                              |
| Analysis specification   | Pre-specified                   |
| Analysis type  | other                           |
| P-value  | < 0.05                          |
| Method   | McNemar                         |
| Parameter estimate   | Odds ratio (OR)                 |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |

## Secondary: Hematuria

|                 |           |
|-----------------|-----------|
| End point title | Hematuria |
|-----------------|-----------|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Hematuria during or within one week after each BTX-A treatment

| End point values            | Alkalinized lidocaine | Placebo         | Alkalinized lidocaine | Placebo         |
|-----------------------------|-----------------------|-----------------|-----------------------|-----------------|
| Subject group type          | Reporting group       | Reporting group | Reporting group       | Reporting group |
| Number of subjects analysed | 25                    | 25              | 21                    | 20              |
| Units: Frequency            | 4                     | 2               | 4                     | 2               |

## Statistical analyses

|                            |               |
|----------------------------|---------------|
| Statistical analysis title | McNemars test |
|----------------------------|---------------|

Statistical analysis description:

McNemars test was used to compare hematuria in the intervention and placebo group.

|   |                                 |
|---|---------------------------------|
| Comparison groups                       | Alkalinized lidocaine v Placebo |
| Number of subjects included in analysis | 45                              |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           | other                           |
| P-value                                 | < 0.05                          |
| Method                                  | Mcnemar                         |
| Parameter estimate                      | Odds ratio (OR)                 |
| Confidence interval                     |                                 |
| level                                   | 95 %                            |
| Variability estimate                    | Standard deviation              |

## Secondary: Clean intermittent catheterization (CIC)

|                 |  |
|-----------------|--|
| End point title | Clean intermittent catheterization (CIC) |
|-----------------|--|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Post-void residuals requiring clean intermittent catheterization (CIC) within one week after BTX-A treatment

| <b>End point values</b>     | Alkalinized lidocaine | Placebo         | Alkalinized lidocaine | Placebo         |
|-----------------------------|-----------------------|-----------------|-----------------------|-----------------|
| Subject group type          | Reporting group       | Reporting group | Reporting group       | Reporting group |
| Number of subjects analysed | 25                    | 25              | 21                    | 20              |
| Units: Frequency            | 1                     | 0               | 0                     | 0               |

## Statistical analyses

|   |                                 |
|---|---------------------------------|
| <b>Statistical analysis title</b>   | McNemars test                   |
| Statistical analysis description:   |                                 |
| McNemars test was used to compare CIC risk in intervention and placebo group. |                                 |
| Comparison groups   | Alkalinized lidocaine v Placebo |
| Number of subjects included in analysis                                       | 45                              |
| Analysis specification  | Pre-specified                   |
| Analysis type   | other                           |
| P-value   | < 0.05                          |
| Method  | McNemar                         |
| Confidence interval   |                                 |
| level   | 95 %                            |
| sides   | 2-sided                         |
| Variability estimate  | Standard deviation              |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were registered on-site during BTX-A treatments or during follow-up calls one week after each BTX-A treatment. Patients were asked about specific adverse events (urinary retention, UTI, hematuria).

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                    |      |
|--------------------|------|
| Dictionary name    | None |
| Dictionary version | 0    |

### Reporting groups

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Alkalinized lidocaine |
|-----------------------|-----------------------|

Reporting group description:

Intervention

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Adverse events were registered on-site during BTX-A treatments or during follow-up calls one week after each BTX-A treatment. Patients were asked about specific adverse events (urinary retention, UTI, hematuria).

| Serious adverse events                            | Alkalinized lidocaine | Placebo        |  |
|---|-----------------------|----------------|--|
| Total subjects affected by serious adverse events |                       |                |  |
| subjects affected / exposed                       | 0 / 48 (0.00%)        | 0 / 45 (0.00%) |  |
| number of deaths (all causes)                     | 0                     | 0              |  |
| number of deaths resulting from adverse events    |                       |                |  |

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

| Non-serious adverse events                            | Alkalinized lidocaine | Placebo          |  |
|---|-----------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                       |                  |  |
| subjects affected / exposed                           | 22 / 48 (45.83%)      | 23 / 45 (51.11%) |  |
| Nervous system disorders                              |                       |                  |  |
| Dizziness   |                       |                  |  |
| subjects affected / exposed                           | 1 / 48 (2.08%)        | 1 / 45 (2.22%)   |  |
| occurrences (all)                                     | 1                     | 1                |  |
| Headache  |                       |                  |  |
| subjects affected / exposed                           | 0 / 48 (0.00%)        | 1 / 45 (2.22%)   |  |
| occurrences (all)                                     | 0                     | 1                |  |
| Reproductive system and breast disorders              |                       |                  |  |

|  |                      |                      |  |
|--|----------------------|----------------------|--|
| Vaginal bleeding<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 48 (0.00%)<br>0  | 1 / 45 (2.22%)<br>1  |  |
| Renal and urinary disorders  |                      |                      |  |
| Dysuria<br>subjects affected / exposed<br>occurrences (all)                              | 7 / 48 (14.58%)<br>7 | 7 / 45 (15.56%)<br>7 |  |
| Bladder pain<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 48 (2.08%)<br>1  | 1 / 45 (2.22%)<br>1  |  |
| Pelvic pain<br>subjects affected / exposed<br>occurrences (all)                          | 1 / 48 (2.08%)<br>1  | 3 / 45 (6.67%)<br>3  |  |
| Pollakiuria<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 48 (0.00%)<br>0  | 2 / 45 (4.44%)<br>2  |  |
| Asymptomatic urinary tract infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 48 (0.00%)<br>0  | 1 / 45 (2.22%)<br>1  |  |
| Urgency urinary incontinence<br>subjects affected / exposed<br>occurrences (all)         | 1 / 48 (2.08%)<br>1  | 0 / 45 (0.00%)<br>0  |  |
| Urethral bleeding<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 48 (0.00%)<br>0  | 1 / 45 (2.22%)<br>1  |  |
| hematuria<br>subjects affected / exposed<br>occurrences (all)                            | 5 / 48 (10.42%)<br>5 | 2 / 45 (4.44%)<br>2  |  |
| Urinary retention<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 48 (2.08%)<br>1  | 0 / 45 (0.00%)<br>0  |  |
| UTI<br>subjects affected / exposed<br>occurrences (all)                                  | 5 / 48 (10.42%)<br>5 | 2 / 45 (4.44%)<br>2  |  |
| Infections and infestations  |                      |                      |  |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| Fever                       |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences (all)           | 0              | 1              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 02 January 2023 | We requested a protocol amendment after enrolling the first three patients in the trial because the treating nurse observed a milky white appearance in the trial medication after mixing. Our initial protocol followed the same solution administered in a previous RCT by, which comprised 20 mL of 2% lidocaine hydrochloride with 10 mL of 8.4% sodium bicarbonate. As a result, the trial was halted due to the compromised double-blind conditions. We consulted the Capital Region of Denmark's unit for pharmaceutical advice. The unit stated that the mixture of lidocaine hydrochloride 20 mg/mL and sodium hydrogen carbonate 1 mmol/mL was unstable and could precipitate. This could lead to reduced anesthetic effect compared to anticipated results. Additionally, the solution could potentially irritate the bladder mucosa. The hospital pharmacy conducted new analyses and recommended dissolving the mixture in 10 mL of sodium chloride (9 g/L). This prevented the milky white appearance or precipitation of the trial medication. Amendment approval for 10 mL sodium chloride was obtained from the Danish Research Ethics Committees and the Danish Medicines Agency. The trial was resumed in January 2023 |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported