



Clinical trial results:

Study of the efficacy and tolerance of intra-prostatic injection of botulinum toxin A in men for the treatment of symptomatic benign prostate hyperplasia.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2010-022255-37 |
| Trial protocol | FR |
| Global end of trial date | 28 April 2015 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 15 January 2022 |
| First version publication date | 15 January 2022 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CHUBX2010/39 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01275521 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | CHU de Bordeaux |
| Sponsor organisation address | 12 rue Dubernat, Talence, France, 33404 |
| Public contact | Dr Grégoire ROBERT, Service d'Urologie, +33 556795547, gregoire.robert@chu-bordeaux.fr |
| Scientific contact | Dr Grégoire ROBERT, Service d'Urologie, +33 556795547, gregoire.robert@chu-bordeaux.fr |

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 | 21 February 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 28 April 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 April 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of intra-prostatic injection of BONT-A in men in the treatment of symptomatic BPH.

Protection of trial subjects:

If an adverse event or a tolerance problem related to intra-prostatic injection of BONT-A occurs outside of the scheduled dates for follow-up visits, patients may consult an investigator at one of the investigating centres.

These emergency consultations will be conducted in the urology department during the hours of consultation or through the out-of-hours emergency department.

These consultations will be conducted to the best of the current state of medical knowledge: depending on the patient's condition, all clinical and complementary examinations necessary to take the patient's in charge may be prescribed.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 10 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 | France: 127 |
| Worldwide total number of subjects | 127 |
| EEA total number of subjects | 127 |

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) | 71 |

| | |
|---------------------|----|
| From 65 to 84 years | 55 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

Date of first inclusion: 10-jan-2011

End date of last included patient: 28-Apr-2015

9 centres (Part of the Committee for Male Mictional Disorders of the French Association of Urology (CTMH-AFU)) in France participated in the study.

Pre-assignment

Screening details:

- Patient aged 50 to 85
- Obstructive or irritative urinary symptomatology linked to a BPH
- Score IPSS moderate to severe (8-19: moderate; 20-35: severe) or IPSS ≤ 7 in patient medically treated for symptomatic BPH
- Increase in prostate volume on the rectal touch or ultrasound
- Free consent

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall 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 | BONT-A intra-prostatic injection |

Arm description:

Intra-prostatic injection of botulinum toxin A

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Botulinum toxin A |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Rectal capsule |
| Routes of administration | Intraprostatic use |

Dosage and administration details:

Single dose of ofloxacin 200mg (or ceftriaxone 1g case of allergy) in accordance with the current recommendations concerning biopsies prostate.

Intra-prostatic injection of 200 IU BONT-A (to be diluted in 10 cc of isotonic saline), divided into 4 injection sites, 2 in each prostatic lobe, respectively 2.5 cc each.

| | |
|------------------|---------------------------------|
| Arm title | Optimized medical BPH treatment |
|------------------|---------------------------------|

Arm description:

Optimized medical BPH treatment

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Other |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Buccal tablet |
| Routes of administration | Buccal use |

Dosage and administration details:

This medical treatment can include the prescription of herbal medicine, alpha-blocker, 5 alpha reductase inhibitor, or combination of alpha-blocker and 5-alpha reductase inhibitor.

| Number of subjects in period 1 | BONT-A intra-prostatic injection | Optimized medical BPH treatment |
|---------------------------------------|----------------------------------|---------------------------------|
| Started | 64 | 63 |
| Completed | 45 | 46 |
| Not completed | 19 | 17 |
| Consent withdrawn by subject | 16 | 12 |
| Other reasons | 2 | 4 |
| Lost to follow-up | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|--|----------------------------------|
| Reporting group title | BONT-A intra-prostatic injection |
| Reporting group description: Intra-prostatic injection of botulinum toxin A | |
| Reporting group title | Optimized medical BPH treatment |
| Reporting group description: Optimized medical BPH treatment | |

| Reporting group values | BONT-A intra-prostatic injection | Optimized medical BPH treatment | Total |
|--|----------------------------------|---------------------------------|-------|
| Number of subjects | 64 | 63 | 127 |
| 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) | | | 71 |
| From 65-84 years | | | 55 |
| 85 years and over | | | 1 |
| Age continuous Units: years | | | |
| arithmetic mean | 65.2 | 64.3 | |
| standard deviation | ± 7.3 | ± 7.6 | - |
| Gender categorical Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 64 | 63 | 127 |

Subject analysis sets

| | |
|--|---|
| Subject analysis set title | Per protocol BONT-A intra-prostatic injection |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Population analysed under treatment | |
| Subject analysis set title | Per protocol Optimized medical BPH treatment |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Population analysed under treatment | |
| Subject analysis set title | Intention-to-treat BONT-A intra-prostatic injection |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Population analysed by intention-to-treat | |
| Subject analysis set title | Intention-to-treat Optimized medical BPH treatment |

| | |
|---|--------------------|
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Population analysed in intention-to-treat | |

| Reporting group values | Per protocol BONT-A intra-prostatic injection | Per protocol Optimized medical BPH treatment | Intention-to-treat BONT-A intra-prostatic injection |
|---|---|--|---|
| Number of subjects | 44 | 60 | 64 |
| 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 | 65.2 | 64.3 | 65.2 |
| standard deviation | ± 7.3 | ± 7.6 | ± 7.3 |
| Gender categorical Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 44 | 60 | 64 |

| Reporting group values | Intention-to-treat Optimized medical BPH treatment | | |
|---|--|--|--|
| Number of subjects | 63 | | |
| 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 | 64.3 | | |
| standard deviation | ± 7.6 | | |
| Gender categorical Units: Subjects | | | |
| Female | 0 | | |

| | | | |
|------|----|--|--|
| Male | 63 | | |
|------|----|--|--|

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | BONT-A intra-prostatic injection |
| Reporting group description: Intra-prostatic injection of botulinum toxin A | |
| Reporting group title | Optimized medical BPH treatment |
| Reporting group description: Optimized medical BPH treatment | |
| Subject analysis set title | Per protocol BONT-A intra-prostatic injection |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Population analysed under treatment | |
| Subject analysis set title | Per protocol Optimized medical BPH treatment |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Population analysed under treatment | |
| Subject analysis set title | Intention-to-treat BONT-A intra-prostatic injection |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Population analysed by intention-to-treat | |
| Subject analysis set title | Intention-to-treat Optimized medical BPH treatment |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Population analysed in intention-to-treat | |

Primary: Evaluation of the patient with auto-questionnaire IPSS urinary symptomatology: questions 1 to 7 (0 to 35 score)

| | |
|---|---|
| End point title | Evaluation of the patient with auto-questionnaire IPSS urinary symptomatology: questions 1 to 7 (0 to 35 score) |
| End point description: Evaluation of the patient's urinary symptomatology by International Prostate Symptom Score (IPSS) self-assessment questionnaire with questions 1-7 assessing obstructive and irritative symptoms related to BPH (8-19 moderate, 20-35 severe) | |
| End point type | Primary |
| End point timeframe: At 4 months after the study inclusion | |

| End point values | Per protocol BONT-A intra-prostatic injection | Per protocol Optimized medical BPH treatment | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 44 | 60 | | |
| Units: score | | | | |
| arithmetic mean (standard deviation) | 12.3 (± 7.4) | 12.0 (± 6.9) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Difference in mean IPSS score [0-35] |
| Statistical analysis description: The analysis use the multiple imputation strategy with adjustment for exposure to 5 alpha-reductase inhibitor (ARI) treatment and IPSS score at M0 | |
| Comparison groups | Per protocol Optimized medical BPH treatment v Per protocol BONT-A intra-prostatic injection |
| Number of subjects included in analysis | 104 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Method | t-test, 2-sided |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.14 |
| upper limit | 2.11 |

Secondary: IPSS question 8 (score 0 to 6)

| | |
|--------------------------------------|--------------------------------|
| End point title | IPSS question 8 (score 0 to 6) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: At 4 months. | |

| End point values | Intention-to-treat BONT-A intra-prostatic injection | Intention-to-treat Optimized medical BPH treatment | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 58 | 53 | | |
| Units: scores | | | | |
| arithmetic mean (standard deviation) | 3.1 (\pm 1.4) | 3.1 (\pm 1.4) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Treatment effect allocated by randomisation |
| Statistical analysis description: Results of the intention-to-treat analysis of the IPSS score at question 8 at M4, with adjustment for the stratification variable of randomisation and the IPSS score at question 8 at M0 | |
| Comparison groups | Intention-to-treat BONT-A intra-prostatic injection v Intention-to-treat Optimized medical BPH treatment |

| | |
|---|--------------------|
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0658 |
| Method | Regression, Linear |
| Parameter estimate | Slope |
| Point estimate | -0.47 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.97 |
| upper limit | 0.03 |

Secondary: Measurement of urine flowmetry Qmax

| | |
|--|-------------------------------------|
| End point title | Measurement of urine flowmetry Qmax |
| End point description: | |
| This endpoint is analysed only in patients with a urine volume \geq 80mL at visit M4 | |
| End point type | Secondary |
| End point timeframe: | |
| At 4 months | |

| End point values | Intention-to-treat BONT-A intra-prostatic injection | Intention-to-treat Optimized medical BPH treatment | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 46 | 41 | | |
| Units: millilitre(s)/seconds | | | | |
| arithmetic mean (standard deviation) | 12.9 (\pm 8.2) | 12.2 (\pm 6.0) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Treatment effect allocated by randomisation |
| Statistical analysis description: | |
| Results of intention-to-treat analysis of Qmax (in mL/s) at M4, with adjustment for the stratification variable of randomisation and Qmax measurement at M0 | |
| Comparison groups | Intention-to-treat BONT-A intra-prostatic injection v Intention-to-treat Optimized medical BPH treatment |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4529 |
| Method | Regression, Linear |
| Parameter estimate | Slope |
| Point estimate | 1.01 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.66 |
| upper limit | 3.69 |

Secondary: Measurement of post-void residual

| | |
|--|-----------------------------------|
| End point title | Measurement of post-void residual |
| End point description: Measurement of post-void residual assessed by suprapubic ultrasound or urinary catheterization evacuator | |
| End point type | Secondary |
| End point timeframe: At 4 months | |

| End point values | Intention-to-treat BONT-A intra-prostatic injection | Intention-to-treat Optimized medical BPH treatment | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 54 | 52 | | |
| Units: millilitre(s) | | | | |
| arithmetic mean (standard deviation) | 59.7 (± 77.2) | 70.3 (± 95.5) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Treatment effect allocated by randomisation |
| Statistical analysis description: Results of intention-to-treat analysis of post-void residual measurements (in mL) at M4, with adjustment for the stratification variable of randomisation | |
| Comparison groups | Intention-to-treat BONT-A intra-prostatic injection v Intention-to-treat Optimized medical BPH treatment |
| Number of subjects included in analysis | 106 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5207 |
| Method | Regression, Linear |
| Parameter estimate | Slope |
| Point estimate | -10.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -44.07 |
| upper limit | 22.45 |

Secondary: Measurement of prostate volume

| | |
|-----------------|--------------------------------|
| End point title | Measurement of prostate volume |
|-----------------|--------------------------------|

End point description:

Measurement of prostate volume assessed by endorectal ultrasound

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

End point timeframe:

At 4 months

| End point values | Intention-to-treat BONT-A intra-prostatic injection | Intention-to-treat Optimized medical BPH treatment | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 57 | 50 | | |
| Units: millilitre(s) | | | | |
| arithmetic mean (standard deviation) | 58.4 (± 31.4) | 51.8 (± 30.2) | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Treatment effect allocated by randomisation |
|----------------------------|---|

Statistical analysis description:

Results of intention-to-treat analysis of prostate volume measurements (in mL) at M4, with adjustment for the stratification variable of randomisation

| | |
|---|--|
| Comparison groups | Intention-to-treat BONT-A intra-prostatic injection v Intention-to-treat Optimized medical BPH treatment |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2686 |
| Method | Regression, Linear |
| Parameter estimate | Slope |
| Point estimate | 6.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.21 |
| upper limit | 18.53 |

Secondary: Evaluation of erectile function using the IIEF-5 self-assessment questionnaire (score from 0 to 24)

| | |
|-----------------|--|
| End point title | Evaluation of erectile function using the IIEF-5 self-assessment |
|-----------------|--|

| | |
|---|------------------------------------|
| | questionnaire (score from 0 to 24) |
| End point description: | |
| Evaluation of erectile function using the International Index of Erectile Dysfunction score (IIEF-5) self-assessment questionnaire (score from 0 to 24) | |
| End point type | Secondary |
| End point timeframe: | |
| At 4 months | |

| End point values | Intention-to-treat BONT-A intra-prostatic injection | Intention-to-treat Optimized medical BPH treatment | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 58 | 53 | | |
| Units: scores | | | | |
| arithmetic mean (standard deviation) | 14.9 (± 8.3) | 14.1 (± 7.7) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Treatment effect allocated by randomisation |
| Statistical analysis description: | |
| Results of ITT analysis of IIEF-5 score at M4, with adjustment for randomisation stratification variable | |
| Comparison groups | Intention-to-treat Optimized medical BPH treatment v Intention-to-treat BONT-A intra-prostatic injection |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5438 |
| Method | Regression, Linear |
| Parameter estimate | Slope |
| Point estimate | 0.91 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.04 |
| upper limit | 3.85 |

Secondary: Evaluation of urinary continence by ICS 1 scores (score from 0 to 23)

| | |
|---|---|
| End point title | Evaluation of urinary continence by ICS 1 scores (score from 0 to 23) |
| End point description: | |
| Evaluation of urinary continence by Internation Continence Society Score 1 (ICS 1) (score from 0 to 23) | |
| End point type | Secondary |
| End point timeframe: | |
| At 4 months | |

| End point values | Intention-to-treat BONT-A intra-prostatic injection | Intention-to-treat Optimized medical BPH treatment | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 58 | 53 | | |
| Units: scores | | | | |
| arithmetic mean (standard deviation) | 1.1 (\pm 2.2) | 0.6 (\pm 1.5) | | |

Statistical analyses

| Statistical analysis title | Treatment effect allocated by randomisation |
|--|--|
| Statistical analysis description: | |
| Results of intention-to-treat analysis of ICS1 score at M4, with adjustment for randomisation stratification variable and ICS1 score at M0 | |
| Comparison groups | Intention-to-treat BONT-A intra-prostatic injection v Intention-to-treat Optimized medical BPH treatment |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.789 |
| Method | Regression, Linear |
| Parameter estimate | Slope |
| Point estimate | 0.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.37 |
| upper limit | 0.49 |

Secondary: Evaluation of urinary continence by ICS 2 scores (score from 0 to 12)

| | |
|------------------------|---|
| End point title | Evaluation of urinary continence by ICS 2 scores (score from 0 to 12) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| At 4 months | |

| End point values | Intention-to-treat BONT-A intra-prostatic injection | Intention-to-treat Optimized medical BPH treatment | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 58 | 53 | | |
| Units: scores | | | | |
| arithmetic mean (standard deviation) | 1.2 (\pm 2.4) | 0.7 (\pm 1.9) | | |

Statistical analyses

| Statistical analysis title | Effect of treatment allocated by randomisation |
|--|--|
| Statistical analysis description: | |
| Results of intention-to-treat analysis of ICS2 score at M4, with adjustment for randomisation stratification variable and ICS2 score at M0 | |
| Comparison groups | Intention-to-treat BONT-A intra-prostatic injection v Intention-to-treat Optimized medical BPH treatment |
| Number of subjects included in analysis | 111 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4458 |
| Method | Regression, Linear |
| Parameter estimate | Slope |
| Point estimate | 0.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.37 |
| upper limit | 0.83 |

Secondary: Need for surgical intervention

| | |
|------------------------|--------------------------------|
| End point title | Need for surgical intervention |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| At 4 months | |

| End point values | Per protocol BONT-A intra- prostatic injection | Per protocol Optimized medical BPH treatment | | |
|-----------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 44 | 60 | | |
| Units: percent | | | | |
| number (not applicable) | | | | |
| Yes | 4.5 | 8.3 | | |
| No | 95.5 | 91.7 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall study

Adverse event reporting additional description:

These adverse events described by PT occurred during follow-up (before and after M4)

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------------------|
| Reporting group title | BONT-A intra-prostatic injection |
|-----------------------|----------------------------------|

Reporting group description: -

| | |
|-----------------------|---------------------------------|
| Reporting group title | Optimized medical BPH treatment |
|-----------------------|---------------------------------|

Reporting group description: -

| Serious adverse events | BONT-A intra-prostatic injection | Optimized medical BPH treatment | |
|---|--|---------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 18 / 64 (28.13%) | 15 / 63 (23.81%) | |
| number of deaths (all causes) | 1 | 0 | |
| number of deaths resulting from adverse events | 1 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of prostate (10001186) | Additional description: Adenocarcinoma of prostate (10001186) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelodysplasia (10028532) | Additional description: Myelodysplasia (10028532) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma of lung (10041826) | Additional description: Squamous cell carcinoma of lung (10041826) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Vascular disorders | | | |

| | | | |
|---|--|----------------|--|
| Critical limb ischemia (10058069) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Critical limb ischemia (10058069) | | |
| | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| | 0 / 1 | 0 / 0 | |
| | 0 / 0 | 0 / 0 | |
| Hypotension (10021097) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Hypotension (10021097) | | |
| | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| | 0 / 1 | 0 / 0 | |
| | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures Anoplasty (10068132) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Anoplasty (10068132) | | |
| | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| | 0 / 1 | 0 / 0 | |
| | 0 / 0 | 0 / 0 | |
| Diabetic diet (10064725) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Diabetic diet (10064725) | | |
| | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| | 0 / 0 | 0 / 1 | |
| | 0 / 0 | 0 / 0 | |
| Hospitalisation (10054112) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Hospitalisation (10054112) | | |
| | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| | 0 / 1 | 0 / 0 | |
| | 0 / 0 | 0 / 0 | |
| Hernia hiatus repair (10019915) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Hernia hiatus repair (10019915) | | |
| | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| | 0 / 1 | 0 / 0 | |
| | 0 / 0 | 0 / 0 | |
| Knee prosthesis insertion (10050155) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Knee prosthesis insertion (10050155) | | |
| | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| | 0 / 2 | 0 / 0 | |
| | 0 / 0 | 0 / 0 | |
| Laser prostatectomy (10023925) subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Laser prostatectomy (10023925) | | |
| | 1 / 64 (1.56%) | 2 / 63 (3.17%) | |
| | 0 / 1 | 0 / 2 | |
| | 0 / 0 | 0 / 0 | |

| | | | |
|--|--|----------------|--|
| Prostate adenoma removal (10065313) | Additional description: Prostate adenoma removal (10065313) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Removal of foreign body (10062102) | Additional description: Removal of foreign body (10062102) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toe amputation (10043913) | Additional description: Toe amputation (10043913) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transurethral prostatectomy (10044445) | Additional description: Transurethral prostatectomy (10044445) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 2 / 63 (3.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Asthenia (10003549) | Additional description: Asthenia (10003549) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cyst (10011732) | Additional description: Cyst (10011732) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Acute prostatitis (10001021) | Additional description: Acute prostatitis (10001021) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erection decreased (10015117) | Additional description: Erection decreased (10015117) | | |

| | | | |
|---|---|----------------|--|
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatitis (10036978) | Additional description: Prostatitis (10036978) | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Epistaxis (10015090) | Additional description: Epistaxis (10015090) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Depression (10012378) | Additional description: Depression (10012378) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Major depression (10057840) | Additional description: Major depression (10057840) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Biopsy of prostate (10004825) | Additional description: Biopsy of prostate (10004825) | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood creatine phosphokinase increased (10005470) | Additional description: Blood creatine phosphokinase increased (10005470) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| AFib (10001452) | Additional description: AFib (10001452) | | |

| | | | |
|---|--|----------------|--|
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular tachycardia (10047302) | Additional description: Ventricular tachycardia (10047302) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Carotid artery stenosis (10007687) | Additional description: Carotid artery stenosis (10007687) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia (10016288) | Additional description: Febrile neutropenia (10016288) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia (10029354) | Additional description: Neutropenia (10029354) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Eye haemorrhage (10015926) | Additional description: Eye haemorrhage (10015926) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Pyrosis (10037676) | Additional description: Pyrosis (10037676) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectorrhagia (10063014) | Additional description: Rectorrhagia (10063014) | | |

| | | | |
|---|--|----------------|--|
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Haematuria (10018867) | Additional description: Haematuria (10018867) | | |
| subjects affected / exposed | 3 / 64 (4.69%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal colic (10038419) | Additional description: Renal colic (10038419) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention (10046555) | Additional description: Urinary retention (10046555) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 2 / 63 (3.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Ankylosing spondylitis (10002556) | Additional description: Ankylosing spondylitis (10002556) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dupuytren's contracture (10013872) | Additional description: Dupuytren's contracture (10013872) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | BONT-A intra-prostatic injection | Optimized medical BPH treatment | |
|---|---|---------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 33 / 64 (51.56%) | 28 / 63 (44.44%) | |
| Vascular disorders | | | |
| Essential hypertension (10015488) | Additional description: Essential hypertension (10015488) | | |

| | | | |
|--|---|----------------|--|
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypotension (10021097) | Additional description: Hypotension (10021097) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Peripheral obliterative arteriopathy (10072121) | Additional description: Peripheral obliterative arteriopathy (10072121) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Surgical and medical procedures | | | |
| Bladder tumour resection (10005085) | Additional description: Bladder tumour resection (10005085) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| Asthenia (10003549) | Additional description: Asthenia (10003549) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Fatigue (10016256) | Additional description: Fatigue (10016256) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nodule (10054107) | Additional description: Nodule (10054107) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Pyrexia (10037660) | Additional description: Pyrexia (10037660) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Immune system disorders | | | |
| Allergy (10001738) | Additional description: Allergy (10001738) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Reproductive system and breast disorders | | | |
| Anejaculation (10073936) | Additional description: Anejaculation (10073936) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ejaculation failure (10014328) | Additional description: Ejaculation failure (10014328) | | |

| | | | |
|---|---|---------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 64 (1.56%) 1 | 6 / 63 (9.52%) 6 | |
| Ejaculation disorder (10014326) | Additional description: Ejaculation disorder (10014326) | | |
| subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 1 / 63 (1.59%) 1 | |
| Erection decreased (10015117) | Additional description: Erection decreased (10015117) | | |
| subjects affected / exposed occurrences (all) | 1 / 64 (1.56%) 1 | 4 / 63 (6.35%) 4 | |
| Gynaecomastia (10018800) | Additional description: Gynaecomastia (10018800) | | |
| subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 1 / 63 (1.59%) 1 | |
| Haemospermia (10019025) | Additional description: Haemospermia (10019025) | | |
| subjects affected / exposed occurrences (all) | 5 / 64 (7.81%) 5 | 0 / 63 (0.00%) 0 | |
| Painful ejaculation (10072353) | Additional description: Painful ejaculation (10072353) | | |
| subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 1 / 63 (1.59%) 1 | |
| Prostatitis (10036978) | Additional description: Prostatitis (10036978) | | |
| subjects affected / exposed occurrences (all) | 5 / 64 (7.81%) 5 | 1 / 63 (1.59%) 1 | |
| Retrograde ejaculation (10038967) | Additional description: Retrograde ejaculation (10038967) | | |
| subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 2 / 63 (3.17%) 2 | |
| Testicular pain (10043345) | Additional description: Testicular pain (10043345) | | |
| subjects affected / exposed occurrences (all) | 0 / 64 (0.00%) 0 | 1 / 63 (1.59%) 1 | |
| Psychiatric disorders | | | |
| Libido decreased (10024419) | Additional description: Libido decreased (10024419) | | |
| subjects affected / exposed occurrences (all) | 2 / 64 (3.13%) 2 | 3 / 63 (4.76%) 3 | |
| Insomnia (10022437) | Additional description: Insomnia (10022437) | | |
| subjects affected / exposed occurrences (all) | 1 / 64 (1.56%) 1 | 0 / 63 (0.00%) 0 | |
| Investigations | | | |
| Elevated prostate specific antigen [PSA] (10014484) | Additional description: Elevated prostate specific antigen [PSA] (10014484) | | |

| | | | |
|--|--|----------------|--|
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Prostate specific antigen increased (10036931) | Additional description: Prostate specific antigen increased (10036931) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Semen volume decreased (10039944) | Additional description: Semen volume decreased (10039944) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 3 / 63 (4.76%) | |
| occurrences (all) | 0 | 3 | |
| Congenital, familial and genetic disorders | | | |
| Hydrocele (10020488) | Additional description: Hydrocele (10020488) | | |
| subjects affected / exposed | 2 / 64 (3.13%) | 0 / 63 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Cardiac disorders | | | |
| Arrhythmia (10003119) | Additional description: Arrhythmia (10003119) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Bradycardia (10006093) | Additional description: Bradycardia (10006093) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Palpitation (10033556) | Additional description: Palpitation (10033556) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 2 / 63 (3.17%) | |
| occurrences (all) | 0 | 3 | |
| Nervous system disorders | | | |
| Dizziness (10013573) | Additional description: Dizziness (10013573) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 1 | 1 | |
| Headache (10019211) | Additional description: Headache (10019211) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 3 / 63 (4.76%) | |
| occurrences (all) | 1 | 3 | |
| Parasthesia (10033922) | Additional description: Parasthesia (10033922) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Syncope vasovagal (10042777) | Additional description: Syncope vasovagal (10042777) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|--|--|----------------|--|
| Eye disorders | | | |
| Eye allergy (10015907) | Additional description: Eye allergy (10015907) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorders | | | |
| Digestion impaired (10012980) | Additional description: Digestion impaired (10012980) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Dryness oral (10013794) | Additional description: Dryness oral (10013794) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Haemorrhoids (10019022) | Additional description: Haemorrhoids (10019022) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 2 | 1 | |
| Nausea (10028813) | Additional description: Nausea (10028813) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Urticaria (10046735) | Additional description: Urticaria (10046735) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Renal and urinary disorders | | | |
| Bladder pain (10005063) | Additional description: Bladder pain (10005063) | | |
| subjects affected / exposed | 0 / 64 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 1 | |
| Burning micturition (10006779) | Additional description: Burning micturition (10006779) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dysuria (10013990) | Additional description: Dysuria (10013990) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 1 / 63 (1.59%) | |
| occurrences (all) | 1 | 1 | |
| Haematuria (10018867) | Additional description: Haematuria (10018867) | | |
| subjects affected / exposed | 6 / 64 (9.38%) | 0 / 63 (0.00%) | |
| occurrences (all) | 7 | 0 | |
| Renal colic (10038419) | Additional description: Renal colic (10038419) | | |
| subjects affected / exposed | 1 / 64 (1.56%) | 0 / 63 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|--|---|---------------------|--|
| Urinary tract disorder (10046566) subjects affected / exposed occurrences (all) | Additional description: Urinary tract disorder (10046566) | | |
| | 1 / 64 (1.56%) 1 | 0 / 63 (0.00%) 0 | |
| | | | |
| Urinary incontinence (10046543) subjects affected / exposed occurrences (all) | Additional description: Urinary incontinence (10046543) | | |
| | 1 / 64 (1.56%) 1 | 0 / 63 (0.00%) 0 | |
| | | | |
| Urinary retention (10046555) subjects affected / exposed occurrences (all) | Additional description: Urinary retention (10046555) | | |
| | 5 / 64 (7.81%) 5 | 0 / 63 (0.00%) 0 | |
| | | | |
| Musculoskeletal and connective tissue disorders Degenerative joint disease (10049491) subjects affected / exposed occurrences (all) | Additional description: Degenerative joint disease (10049491) | | |
| | 1 / 64 (1.56%) 1 | 0 / 63 (0.00%) 0 | |
| | | | |
| Infections and infestations Rhinitis (10039083) subjects affected / exposed occurrences (all) Sinusitis (10040753) subjects affected / exposed occurrences (all) Urinary infection (10046544) subjects affected / exposed occurrences (all) Viral infection (10047461) subjects affected / exposed occurrences (all) | Additional description: Rhinitis (10039083) | | |
| | 0 / 64 (0.00%) 0 | 2 / 63 (3.17%) 2 | |
| | Additional description: Sinusitis (10040753) | | |
| | 1 / 64 (1.56%) 1 | 0 / 63 (0.00%) 0 | |
| | Additional description: Urinary infection (10046544) | | |
| | 5 / 64 (7.81%) 5 | 0 / 63 (0.00%) 0 | |
| | Additional description: Viral infection (10047461) | | |
| | 0 / 64 (0.00%) 0 | 1 / 63 (1.59%) 1 | |
| | | | |
| Metabolism and nutrition disorders Gout (10018627) subjects affected / exposed occurrences (all) NIDDM (10029402) subjects affected / exposed occurrences (all) | Additional description: Gout (10018627) | | |
| | 0 / 64 (0.00%) 0 | 1 / 63 (1.59%) 1 | |
| | Additional description: NIDDM (10029402) | | |
| | 1 / 64 (1.56%) 1 | 0 / 63 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 28 February 2011 | Change in the treatment in case of allergy, modification of the flow-chart. |
| 27 July 2011 | Change of recruitment terms. |
| 25 January 2012 | Extension, changes related to vigilance. |
| 19 December 2012 | Extension. |

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/29383480>