The use of a Polycaprolactone Based Bulking Agent for the Treatment of Female Stress Urinary Incontinence, a Pivotal Trial

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The primary objectives of the trial are to:- Evaluate the efficacy of the PCL-based bulking agent treatment as determined by the Stamey Grading System (SGS). The SGS will be determined at baseline, 3, 6, 12, 18, and 24 months follow-up. - Evaluate...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Urinary tract signs and symptoms
Study type	Interventional

Summary

ID

NL-OMON43407

Source
ToetsingOnline

Brief title
A polycaprolactone treatment for SUI

Condition

- Urinary tract signs and symptoms

Synonym
Stress urinary incontinence, urine loss

Research involving
Human

Sponsors and support

Primary sponsor: AQLANE Medical BV

Source(s) of monetary or material Support: AQLANE Medical BV

Intervention

Keyword: Bulking agent, Polycaprolactone, Stress Urinary Incontinence

Outcome measures

Primary outcome

1. Primary analyses

- Primary efficacy analysis

The primary objective of this trial is to assess the treatment efficacy of the PCL-based bulking agents Urolon*-12, Urolon*-24, and Urolon*48 as determined by the SGS.

The efficacy endpoint is a reduction of at least 1 SGS at 3, 6, 12, 18, and 24 months follow-up compared to baseline.

- Primary safety analysis

The primary objective of this trial is to evaluate the safety of the PCL-based bulking agents Urolon*-12, Urolon*-24, and Urolon*48. Counts and rates of treatment-related AE*s and serious AE*s will be presented after treatment (baseline) and at the 3, 6, 12, 18, and 24 month follow-up time points.

Secondary outcome

2. Secondary analyses

- Secondary efficacy analysis

The secondary objective of this trial is to assess the efficacy and improvement

in patients QoL after treatment with the PCL-based bulking agents Urolon*-12, Urolon*-24, and Urolon*48 as determined with the I-QoL, ICIQ-SF, PGI-I, PGI-S, and non-invasive cough-test.

The efficacy and QoL endpoints are improvement at 3, 6, 12, 18 (no cough-test at this time-point), and 24 months follow-up compared to baseline with the use of the I-QoL, ICIQ-SF, PGI-I, PGI-S, and non- invasive cough-test. The non-invasive cough-test will be performed after treatment to test post-treatment success.

- Secondary efficacy and safety analysis

The secondary objective of this trial is to assess the long-term safety and efficacy which will be assessed by extending the follow-up visits annually up to 5 years. (SGS, I-QoL, PGI-I, PGI-S, and ICIQ-SF). Evaluate safety via an additional cystoscopic examination at 12 and 24 months follow-up

Study description

Background summary

Stress urinary incontinence (SUI) is an involuntary leakage of urine resulting from increased intra-abdominal pressure such as coughing, laughing, sneezing, lifting, running, or changing of body position from horizontal to vertical and may be caused by urethral hypermobility or intrinsic sphincter deficiency (ISD). It is suggested that the cause of ISD lies in weakened urethral sphincter muscles and is the inability of the urethra to provide adequate urethral closure pressure that prevents involuntary loss of urine during increases in abdominal pressure. Additionally, altered collagen production has also been suggested to contribute to SUI. The main constituent in the ligaments and the sub-urethral wall is fibrous connective tissue. Collagen of types I,

III, and VI are the predominant component of this connective tissue. It has been found that women with urinary incontinence have an altered connective tissue metabolism causing decreased collagen production, which may result in insufficient support of the urogenital tract. Activation of collagen production by bulking agents due to neocollagenesis may contribute to a long lasting natural way of increasing support of the urogenital tract.
There is a wide spectrum of treatment options available for SUI, including conservative non-surgical therapy (pelvic floor muscle training, electric stimulation, fluid and dietary, and drug therapy) and surgical procedures. The most commonly used surgical treatment for SUI is the mid-urethral sling procedure; the retropubic (tension-free vaginal tapes (TVT) or the transoburator sling (tension-free vaginal tapes obturator (TVT-O). According to literature, the reported complication rates range from 4.3% to 75.1% for retropubic, and 10.5% to 31.3% for transobturator mid urethral slings. Due to the high complication rate there is a need for less invasive treatments for SUI. Bulking agents are very promising as a minimally invasive therapy because they may be performed under local anesthesia in an outpatient setting, have a low complication rate, have shorter procedure time, shorter inpatient stay and more rapid recovery.

Study objective

The primary objectives of the trial are to:
- Evaluate the efficacy of the PCL-based bulking agent treatment as determined by the Stamey Grading System (SGS). The SGS will be determined at baseline, 3, 6, 12, 18, and 24 months follow-up.
- Evaluate the safety of the PCL-based bulking agent treatment via any reported adverse events at baseline, 3, 6, 12, 18, and 24 months follow-up.

The secondary objectives of the trial are to:
- Evaluate the effect on Quality of Life (QoL) after the PCL-based bulking agent treatment. QoL will be determined with the use of Incontinence Quality of Life questionnaire (I-QoL). The I-QoL will be determined at baseline and at 3, 6, 12, 18, and 24 months follow-up.
- Evaluate the efficacy after the PCL-based bulking agent treatment. Efficacy will be determined with the use of the International Consultation on Incontinence Questionnaire - Short Form (ICIQ-SF). The ICIQ-SF will be determined at baseline and at 3, 6, 12, 18, and 24 months follow-up.
- Evaluate the efficacy after the PCL-based bulking agent treatment. Efficacy will be determined with the use of the Patient*s Global Impression of Improvement scale (PGI-I) and Patient*s Global Impression of Severity scale (PGI-S). The PGI-I will be determined at 3, 6, 12, 18, and 24 months follow-up. The PGI-S will be determined at baseline, 3, 6, 12, 18, and 24 months follow-up.
- Evaluate efficacy as determined by the non-invasive cough test. The non-invasive cough test will be performed at baseline, after treatment, and at 3, 6, 12, and 24 months follow-up.
- Evaluate safety via an additional cystoscopic examination at 12 and 24 months

follow-up.
- Long-term safety and efficacy will be assessed by extending the follow-up visits annually up to 5 years (SGS, I-QoL, PGI-I, PGI-S, and ICIQ-SF).

Study design

This is a prospective pivotal trial to study the safety and efficacy of a PCL-based bulking agent (Urolon*) for stress urinary incontinence (SUI).

Intervention

Eligible subjects will receive injections of the PCL-based bulking agent (Urolon*-12, Urolon*-24, or Urolon*-48). The use of topical, spinal, or general anesthesia is permitted at the discretion of the Investigator. The PCL-based bulking agent injection will be administered into the submucosa of the urethra at the bladder neck using the transurethral technique. Three injections (2, 6, and 10 o*clock positions) will be administered in order to achieve optimal coaptation of the urethral mucosa. A second injection only with the corresponding PCL-based bulking agent (Urolon*-12, Urolon*-24, or Urolon*-48) used for initial treatment is permitted if the patient was not dry after the first treatment. If required, a second injection is permitted at 3 month follow-up and or trial exit.

Study burden and risks

At baseline, 3, 6, 12, 18, and 24 months post treatment the treated subjects have an assessment of safety and efficacy as determined by subjective and objective methods. Long-term safety and efficacy will be assessed by extending the follow-up visits annually up to 5 years (SGS, I-QoL, PGI-I, PGI-S, and ICIQ-SF).

Expected side effects, risks, and/or discomforts are:

1. mild (treatment related) (short term) complications:

• urinary tract infection,
• haematuria,
• dysuria,
• urinary retention,
• urgency,
• headaches,
• pain,
• risks associated with anesthesia, outlet obstruction (slow prolonged stream),
• fever,

2. rare severe (long term) complications:

• periurethral granuloma,
• erosion
• dislocation,
• embolization,
• urethral prolapse,
• formation of abscesses, cysts, and other masses.
• worsening of incontinence

There may be other procedure or device related problems that are not known yet. If during the trial new information becomes available about other problems, every effort will be made to inform the patient.

The patient will receive the best medical care available during and after this trial, but because this is still a clinical trial, unexpected side effects may occur. In the unlikely event that the patient experiences any research-related harm as a result of taking part in this trial, the patient will be provided with medical treatment/care at no cost to the patient. The term *research-related harm* means both physical and mental injury caused by the trial device or trial procedures required by the trial.

Contacts

Public
AQLANE Medical BV

Yalelaan 1
Utrecht 3584 CL
NL
Scientific
AQLANE Medical BV

Yalelaan 1
Utrecht 3584 CL
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Subjects 18 years of age or older
2. Subjects with predominant SUI as determined by the Questionnaire for Urinary Incontinence Diagnosis (QUID); Total Stress score (Sum Q1-3) of >= 4 and Total Urge score (Sum Q4-6) of < 6.
3. Subjects who attempted or failed prior noninvasive pelvic muscle rehabilitation treatment while incontinent.
4. Subjects with mild to moderate SUI as confirmed by SGS 1 or 2
5. Subjects willing and able to comply with study follow-up procedures and schedule
6. Subjects willing to provide written informed consent for their participation in the trial

Exclusion criteria

1. Subjects who have received previous bulking agent implantation in the submucosa of the urethra or had any form of surgery to treat SUI
2. Subjects with any form of urinary incontinence other than predominant SUI
3. Subjects with urinary retention (postvoid residual volume >=100ml)
4. Subjects with morbid obesity (body mass index (BMI) >=40 kg/m2)
5. Subjects with known allergies to antibiotics
6. Subjects with a neurogenic bladder
7. Subjects who were treated with chemotherapy agents or systemic corticosteroids within 3 months prior to enrollment
8. Subjects with a history of autoimmune disorder
9. Subjects with known allergies to topical, injectable, or general anesthetics
10. Subjects with severe allergies manifested by a history of anaphylaxis or those with severe, chronic allergies (e.g. asthma)
11. Subjects with a known bleeding disorder
12. Subjects with an active infection of any kind at the time of enrollment
13. Subjects with known connective tissue disease
14. Subjects who do not agree to use contraceptives throughout the initial 12 months of the trial
15. Subjects who are pregnant (or within 12 months postpartum) or lactating
16. Subjects who are unwilling and/or unable to comply trial follow-up procedures and schedules
17. Subjects enrolled in another investigational clinical trial
18. Subjects with co-morbidities

19. Subjects with non-viable tissue, e.g. history of significant pelvic irradiation, multiple pelvic surgeries, etc. (scar tissue and significantly compromised tissue will not coapt appropriately)
20. Subjects with urethral or bladder neck strictures (use of bulking agents in patients with strictures may cause injury and/or urethral obstruction)
21. Subjects with peripheral vascular disease and/or prior pelvic surgery may be at increased risk for tissue erosion

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-10-2016
Enrollment:	35
Type:	Actual

Medical products/devices used

Generic name:	The PCL-based urethral bulking agent device (Urolon)
Registration:	No

Ethics review

Approved WMO Date:	14-04-2016
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-06-2016

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-07-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-11-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-11-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-02-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL55843.100.15