A Double blind, Randomized, Placebo-Controlled Study Evaluating the Safety and Effectiveness of Cook MyoSite Incorporated AMDC in Female Patients with Stress Urinary Incontinence

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The study will evaluate the injection of AMDC for Urinary Sphincter Repair (USR) compared to a placebo dose, with the hypothesis that one or two treatments of AMDC is statistically superior to placebo at 12 months following the initial treatment.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Urinary tract signs and symptoms
Study type	Interventional

Summary

ID

NL-OMON39970

Source
ToetsingOnline

Brief title
Study investigating CMI autologous muscle-derived cells in women

Condition

- Urinary tract signs and symptoms

Synonym
bladder leakage, Loss of urine on effort

Research involving
Human

Sponsors and support

Primary sponsor: William Cook Europe, Regulatory Affairs, Clinical
Source(s) of monetary or material Support: Cook MyoSite;Inc.

Intervention

Keyword: cell, Incontinence, stress-leaks, urinary

Outcome measures

Primary outcome

The principle objective of the study is to determine the effectiveness and safety of Autologous Muscle-Derived Cells (AMDC) in the treatment of female patients with stress urinary incontinence.

Effectiveness: Is treatment with AMDC effective at 12 months after treatment in reducing the number of stress incontinence episodes or reducing the pad weight?

Safety: Are the side effects or medical events associated with AMDC treatment compared to the benefit acceptable after 12 months?

Secondary outcome

For secondary objectives, the study will examine if effectiveness is maintained long term (2 years). The study will also look at how the AMDC treatment affects the quality of life of the patients, which will use a number of quality of life assessments. Safety will also be examined at timepoints other than 12 months.

Study description

Background summary

Stress Urinary Incontinence (SUI) is a common condition that primarily affects women. SUI is the involuntary leakage of urine on effort or exertion, or on sneezing or coughing. SUI symptoms can occur for two reasons: 1) loss of support in the pelvic floor or bladder or 2) sphincter muscle (muscle around the urethra) function deficiency.

Current treatments for SUI include surgery for slings or injections of bulking agents. Both of these treatments have some disadvantages. Surgery for slings usually involves general anesthesia, catheters that need to be removed later, and a hospital stay. All of these can be a burden for the patient or cause delays in recovery. Disadvantages of collagen injections include loss of effectiveness, the need for repeat injections, high cost, and allergic responses to collagen. Other substances used for bulking injections include synthetic materials or autologous fat (a patient*s own fat). Although these substances have provided evidence for safety of the injection technique, the success of these materials is hindered by the need for multiple injections, and by migration of material. These disadvantages limit the overall success of injection therapy. Ideally, the most successful agent would be durable, non-immunogenic (does not provoke immune response in recipient) and non-migratory (stays in place).

Cook MyoSite Incorporated Autologous Muscle Derived Cells (AMDC) consists of muscle progenitor cells isolated from skeletal muscle tissue that are subsequently propagated ex vivo. Following propagation it is verified that the cells exhibit attributes of functional muscle cells (demonstrated through a potency assay). Once functionality is verified, the cells are delivered into a tissue structure that is likely to benefit from additional muscle function (e.g. the urethra sphincter).

The proposed study will determine the effectiveness and safety of Cook MyoSite Incorporated Autologous Muscle-Derived Cells (AMDC) in the treatment of SUI in female patients. The study will evalutate the injection of AMDC compared to a placebo dose. It is believed that the cells (AMDC) become part of the tissue where they have been injected. In theory, this may help patients to have more control over urine storage and release (peeing). It may also decrease urinary leakage problems, although this is not guaranteed.

The proposed treatment has some advantages when compared to surgery or bulking agents. Injections with AMDC are designed to be an outpatient procedure that does not require general anesthesia, catheters that need to be removed, or a hospitality stay. The procedures involved are all designed to be completed in a

clinic with local anesthetics. If a catheter is used for any part of the procedure, it does not remain in place, and the patient does not need to have it removed at a later date.

Study objective

The study will evaluate the injection of AMDC for Urinary Sphincter Repair (USR) compared to a placebo dose, with the hypothesis that one or two treatments of AMDC is statistically superior to placebo at 12 months following the initial treatment.

Study design

The study design under consideration is a randomized, double-blind, placebo-controlled, multicenter study to determine the effectiveness and safety of AMDC in the treatment of stress urinary incontinence in female patients. The study will randomize patients to receive one of two doses (placebo or 150 x 10^6 cells) and either one or two treatments. The allocation ratio will be 2:1 (cells: placebo), while one and two treatments are equally allocated (1:1). A patient*s randomization assignment will occur at enrollment. The study will treat a total of 246 patients (164 treated with 150×10^6 AMDC and 82 treated with placebo). Those patients randomized to the two treatment groups will receive the same dosage at the 6 month visit that they received at the initial treatment. Placebo injected patients will be given the opportunity to receive the 150 x 10^6 cell dose following the 12 month evaluation.

Intervention

All eligible patients consenting to study participation will have skeletal muscle tissue harvested using a needle biopsy during an initial outpatient procedure. The harvested muscle tissue will be placed in a hypothermic medium and transported to the manufacturer for processing in their cell processing facility in Pittsburgh, PA, USA. The muscle derived cells (MDC) will be isolated and propagated in culture over several weeks to the final dose of 150 x 10^6 for the cell treated groups.
After reaching the desired concentration, the isolated and expanded AMDC will be frozen and shipped back to the investigating physician. The physician will thaw the product (either the cell dose or the acellular cryogenic medium placebo control as assigned per the randomization) and dilute the sample with an equal volume of physiological saline. The resulting suspension will be injected into the patient*s urethral sphincter in a brief outpatient procedure.

Study burden and risks

Risks of participation in the study include those associated with:

Cellular injection: Rare potential risks include an allergic or immune response to AMDC (cells or components of the final formulation including: bovine proteins, ampicillin, and gentamicin sulfate), and infection. Risk of allergic or immune response to the cells is expected to be minimal due to the use of autologous cells. Risk of allergic response to bovine proteins, ampicillin, and gentamicin sulfate used in AMDC production should be minimal since only trace amounts are expected to be in the final product. The risk of infection is expected to be consistent with similar procedures (e.g. cystoscopy). Additional risks include transient dysuria, urgency, or altered micturition frequency.
Since the side effects of muscle cell injection in the urinary passage on reproduction have not been determined, highly effective methods of contraception should be used for the duration of a patient*s involvement in the trial and for two weeks after the last study visit. The investigator should discuss with their patients appropriate birth control methods (double barrier method) which need to be followed for the period of one month prior to the injection visit and continuing until at least two weeks following the last study visit. If the patient has a positive pregnancy test at the biopsy visit, the study staff is not to biopsy the patient, and the patient is then excluded from the study. Additionally, if the patient has a positive pregnancy test on the day of injection the study staff is likewise instructed not to inject the patient, and the patient is excluded from the study.
Cystoscopy:The risks of cystoscopy are expected to be infrequent, and include the possibility of discomfort, mild cramps, bleeding, excessive trauma, and infection. Side effects that are rare include inability to urinate after the procedure and puncture of the bladder or urethra.
Muscle biopsy: Infrequent potential risks include the possibility of wound infection, hematoma, bleeding, and local pain. Rare potential risks include scarring.
Urinary catheterization: The risks of urinary catheterization are expected to be infrequent and include the possibility of transient inability to void, bleeding (hematuria), discomfort or pain during catheter insertion, cramps, and urinary tract infections.
Venipuncture: The risks from venipuncture include bleeding, discomfort, light-headedness, pain, bruising, and rarely, an infection at the site where blood is drawn.
Additional risks are expected to be comparable to those associated with standard treatment using collagen injections. These include the possibility of urinary retention and infection. In addition, mild reactions such as swelling and local irritation may be associated with topical anesthetics used during the injection procedure.
Because this study includes experimental procedures, not all risks and outcomes can be foreseen.
This study will provide information on the safety and effectiveness of the cellular injection in the therapy of urinary incontinence and may help determine how to improve treatment of urinary incontinence. Other patients in

the future may benefit from the knowledge gained from this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• The patient is female and has primary symptoms af SUI, as confirmed by patient medicai h istory and clinical symptoms, including a focused incontinence evaluation.

Exclusion criteria

• Patient has symptoms af pure urge incontinence as confirmed by basic evaluation af etiology from a patient medical history, including a focused incontinence history.

• Patient has symptoms af mixed urinary incontinence where urge incontinence is the predominant factor.
• Patient has had stress urinary incontinence symptoms less than 6 months prior to signing the informed consent.
• Patient has not previously attempted conservative treatment for at least 1 month prior to signing the informed consent. (Examples of conservative treatment include behavior modifications, bladder exercises, biofeedback, etc.)
• Patient has more than 2 episode af awakening to void during normal sleeping hours.
• Patient cannot be ma intained on a stable dose and/or frequency of medication (including diuretics) known to affect lower urinary tract function, including but not limited to, anticholinergics, tricyclic antidepressants or alpha-adrenergic blockers, for at least 2 weeks prior to randomization or is likely to change during the course af the study.
• Patient is pregnant, lactating, or plans to become pregnant during the course of the study.
• Patient refuses to provide written informed consent.
• Patient is not at least 18 years of age.
• Patient is not available for the follow-up evaluations as required by the protocol.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cells autologous

Ethics review

Approved WMO Date:	10-04-2013
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-11-2013
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-04-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-04-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-05-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
EudraCT	EUCTR2011-003599-35-NL
ClinicalTrials.gov	NCT01382602
CCMO	NL41963.000.13