Restorelle® Transvaginal Mesh versus Native Tissue Repair for Treatment of Pelvic Organ Prolapse

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The aim of this postmarket study is to compare the safety and effectiveness of Coloplast Restorelle® transvaginal mesh products in the treatment of pelvic organ prolapse (POP) to traditional native tissue repair through 36 months of follow-up. This...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Soft tissue therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON46901

Source
ToetsingOnline

Brief title
Restorelle 522 study

Condition

- Soft tissue therapeutic procedures

Synonym
Pelvic Organ Prolapse

Research involving
Human

Sponsors and support

Primary sponsor: Coloplast
Source(s) of monetary or material Support: Pharmaceutical Company

Intervention

Keyword: Pelvic Organ Prolapse, Restorelle®, Transvaginal Mesh

Outcome measures

Primary outcome

Primary Effectiveness Endpoint

The primary effectiveness endpoint is recurrent prolapse defined anatomically as prolapse of the target compartment beyond the hymenal ring, or subjectively as perception of protrusion or bulge of target compartment, or as retreatment (including the introduction of a pessary after index procedure) of pelvic organ prolapse in the target compartment at 12 months. If a subject fails any one of the three components, she will be considered a failure for the primary efficacy endpoint.

Prolapse of the target compartment beyond the hymenal ring will be determined by POP-Q examination by an independent examiner.

Perception of protrusion or bulge of target compartment will be determined by the PFDI-20, question 3 (*Do you usually have a bulge or something falling out that you can see or feel in the vaginal area*) answering *yes* and =2 (i.e. responses of *somewhat*, "moderately* or *quite a bit*).

Retreatment is defined as additional surgical treatment for POP or pessary use in the target compartment since the index procedure. For the purposes of this study surgical treatment is defined as anytime the subject returns to the operating room.

The target compartment is defined as the compartment that meets all inclusion criteria and no exclusion criteria for prolapse. For the treatment group, if

one or more compartments that meets the inclusion criteria for prolapse is not treated with mesh, only the compartment treated with mesh will be considered a target compartment. For the purposes of this protocol, a subject may have more than one target compartment.

Primary Safety Endpoint

The primary safety endpoint is the proportion of device and procedure-related serious adverse events (SAEs) at 12-months as determined by the Clinical Events Committee.

Secondary outcome

The secondary effectiveness endpoints are:

1. Recurrent prolapse defined anatomically as prolapse of the target compartment at or beyond the hymenal ring, or perception of protrusion or bulge of the target compartment, or retreatment (including the introduction of a pessary after index procedure) of pelvic organ prolapse in the target compartment at 12 months.

2. Recurrent prolapse defined anatomically as prolapse of the target compartment beyond the hymenal ring, or perception of protrusion or bulge of the target compartment, or retreatment (including the introduction of a pessary after index procedure) of pelvic organ prolapse in the target compartment at 36 months.

3. Recurrent prolapse defined anatomically as prolapse of the target compartment at or beyond the hymenal ring or perception of protrusion or bulge of the target compartment, or retreatment (including the introduction of a

pessary after index procedure) of pelvic organ prolapse in the target compartment at 36 months.

If a subject fails any one of the three components of the endpoint, she will be considered a failure for the secondary efficacy endpoint.
Prolapse of the target compartment at or beyond the hymenal ring will be determined by POP-Q examination by an independent examiner.
Perception of protrusion or bulge of target compartment will be determined by the PFDI-20, question 3 (*Do you usually have a bulge or something falling out that you can see or feel in the vaginal area*) answering *yes* and =2 (i.e. responses of *somewhat*, "moderately or *quite a bit*).
Retreatment is defined as additional surgical treatment for POP or pessary use in the target compartment since the index procedure. For the purposes of this study surgical treatment is defined as anytime the subject returns to the operating room.
The target compartment is defined as the compartment that meets all inclusion criteria and no exclusion criteria for prolapse. For the treatment group, if one or more compartments that meets the inclusion criteria for prolapse is not treated with mesh, only the compartment treated with mesh will be considered a target compartment. For the purposes of this protocol, a subject may have more than one target compartment.

Secondary Safety Endpoints

Secondary safety endpoints are defined as each of the following set of device

or procedure related adverse events (AEs) of interest of any severity at 36 months as determined by the CEC: mesh erosion into another organ, neuromuscular problems (including groin and leg pain), pelvic pain, mesh exposure in the vagina, infection (by type), stress urinary incontinence (worsening or de novo), urge incontinence (worsening or de novo), difficulty emptying bladder (worsening or de novo) and de novo dyspareunia.

Study description

Background summary

What is Restorelle Direct Fix (Restorelle)?
Restorelle Direct Fix has been cleared for use by the United States Food and Drug Administration (FDA) to treat Pelvic Organ Prolapse (POP). The device has also CE marking, which means that it can also be used within the European Union. It is a non-absorbable mesh that is surgically implanted through the vagina (transvaginally) by a doctor and once implanted into the body is permanent.
The mesh acts as a support to the weak or damaged pelvic muscles to prop up the muscles while new tissue grows into the mesh to provide strength and support, preventing the pelvic organs from pushing into the vagina.
The United States Food and Drug Administration (FDA) has required this study to collect information on the safety and effectiveness of Restorelle Direct Fix and the surgical procedure to implant Restorelle. These results will be compared to safety and effectiveness results with patients who have native tissue repair for their pelvic organ prolapse treatment.
More background is described in the ICF Appendix C.

Study objective

The aim of this postmarket study is to compare the safety and effectiveness of Coloplast Restorelle® transvaginal mesh products in the treatment of pelvic organ prolapse (POP) to traditional native tissue repair through 36 months of follow-up. This data will be used to support the 522 orders issued by the FDA and a potential future call for a PMA.
* The Primary Effectiveness Objective is to assess superiority of transvaginal mesh in the treatment of pelvic organ prolapse compared to native tissue repair at 12 months
* The Primary Safety Objective is to assess non-inferiority of transvaginal

mesh in rates of device and procedure-related serious adverse events following treatment of pelvic organ prolapse compared to native tissue repair at 12 months
* The Secondary Effectiveness Objectives are to assess non-inferiority of transvaginal mesh in the treatment of pelvic organ prolapse compared to native tissue repair at 12 months and 36 months
* The Secondary Safety Objectives are to assess non-inferiority of transvaginal mesh in rates of specific adverse events following treatment of pelvic organ prolapse compared to native tissue repair at 36 months
Additional Objectives:
* To assess changes in quality of life, symptoms and sexual satisfaction associated with surgical reconstruction for pelvic organ prolapse compared to native tissue repair
* To assess the effect of risk factors and comorbidities on clinical outcome
* To assess overall clinical outcomes by compartment and combined compartment stratification

Study design

This study is a prospective, non-randomized, two-cohort, multi-center post-market study comparing Restorelle mesh to native tissue repair (No Mesh) in the treatment of pelvic organ prolapse. Subjects will be followed for 36 months, with scheduled follow-up visits at 2-months, 6 months, 12 months, 18 months, 24 months, and 36 months.

Intervention

Study participants will have their pelvic organ prolapse treated with:
* Restorelle Direct Fix only or
* Native tissue repair only or
* A combination of both Restorelle and native tissue repair

Prior surgery: urine test for infections, and, if applicable, pregnancy test.

Tests taking place per visit:
- pelvic exam * each visit (same as at baseline visit)
- questions asked about health * each visit
- complete up to 7 questionnaires to find out how your patient is doing - at each visit:
* 2 months: one questionnaire
* 6 months: six questionnaires
* 12 months: seven questionnaires
* 18 months: five questionnaires
* 2 years: six questionnaires
* 3 years: six questionnaires

Study burden and risks

Because neither the devices nor procedures being studied in the Restorelle 522 Study are experimental, the doctor will conduct the surgery using his or her standard surgical procedure.

Involvement in the study does not add surgical risks, but the surgery is major surgery which includes risks and the doctor will review the risks with the patient. Additionally, the devices and surgery may involve risks which are currently unknown.

During the study visits, several questionnaires have to be filled out which will ask very personal questions. There is a risk that answering these questions may makes the patient feel embarrassed or uncomfortable.

The patient will visit the site 6 times in 3 years, where standard of care would provide only 1 follow-up visit, though there is a trend in most Dutch hospitals that this is already extended to the same 3 years after surgery.

Contacts

Public
Coloplast

West River Rd N 1601
Minneapolis MN 55411
US
Scientific
Coloplast

West River Rd N 1601
Minneapolis MN 55411
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Subject is female
2. Subject is at least 18 years of age
3. Subject has pelvic organ prolapse with leading edge at or beyond the hymen. At or beyond the hymen is defined as POP-Q scores of Ba *0 and C* -1/2 tvl or Bp *0 and C* -1/2 tvl
4. Subject reports a bothersome bulge they can see or feel per PFDI-20 question 3, response of 2 or higher (i.e. responses of *somewhat*, "moderately or *quite a bit*)
5. Subject is willing to provide written informed consent
6. Subject is willing and able to comply with the follow-up regimen

Exclusion criteria

1. Subject is pregnant or intends to become pregnant during the study
2. Subject has an active or chronic systemic infection including any gynecologic infection, untreated urinary tract infection (UTI), or tissue necrosis
3. Subject has a history of pelvic organ cancer (e.g. uterine, ovarian, bladder, or cervical)
4. Subject has had prior or is currently undergoing radiation, laser therapy, or chemotherapy in the pelvic area
5. Subject has taken systemic steroids (within the last month), or immunosuppressive or immunomodulatory treatment (within the last 3 months)
6. Subject has a systemic connective tissue disease (e.g. scleroderma, systemic lupus erythematosus (SLE), Marfan syndrome, Ehlers Danlos, collagenosis, polymyositis or polymyalgia rheumatica)
7. Subject has chronic systemic pain that includes the pelvic area or chronic focal pain that involves the pelvis
8. Subject has uncontrolled diabetes mellitus (DM)
9. Subject has a known neurologic or medical condition affecting bladder function (e.g. multiple sclerosis, spinal cord injury, or stroke with residual neurologic deficit)
10. Subject is seeking obliterative vaginal surgery as treatment for pelvic organ prolapse (colpocleisis)
11. Subject is not able to conform to the modified dorsal lithotomy position
12. Subject is currently participating in or plans to participate in another device or drug study during this study
13. Subject has a known sensitivity to polypropylene (Restorelle mesh arm only)
14. Subject has had previous prolapse repair with mesh in the target compartment(s)
15. Subject is planning to undergo a concomitant prolapse repair in a non-target compartment with anything other than native tissue repair

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-09-2016
Enrollment:	123
Type:	Actual

Medical products/devices used

Generic name:	Restorelle
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	13-09-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-10-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-11-2016
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-07-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
ClinicalTrials.gov	NCT02162615
CCMO	NL56561.018.16