Ulipristal versus Gonadotropin-releasing hormone agonists prior to laparoscopic myomectomy: a double blind randomized controlled trial

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Objective: to investigate if Ulipristal is non-inferior to GnRH in terms of intra-operative blood-loss (primary outcome), surgical time, surgical ease, complications, quality of life and costs.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive neoplasms female benign
Study type	Interventional

Summary

ID

NL-OMON45087

Source
ToetsingOnline

Brief title
Ulipristal vs GnRHa before laparoscopic myomectomy

Condition

- Reproductive neoplasms female benign

Synonym
fibroids, myoma

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Gedeon Richter

Intervention

Keyword: Fibroid, GnRH, Laparoscopy, Ulipristal

Outcome measures

Primary outcome

Total blood loss during laparoscopic myomectomy will be our main study parameter.

Null-hypothesis: Ulipristal is non-inferior to GnRHa in terms of blood loss during surgery when the average difference between the two groups is below 150 ml (standard deviation 250 ml).

Secondary outcome

Secondary outcomes parameters will be reduction of fibroid volume after pre-treatment assessed by 3 dimensional ultrasound (possibility to perform detailed volume assessments afterwards), hemoglobin levels pre- and post operatively, conversion rate to laparotomy, complication rate, re-intervention rate, operative time, surgical ease (see table beneath tis paragraph), breaching of uterine cavity, pain scores and use of analgesia post operatively, quality of life during pre-operative treatment and post-operatively up till 6 months. The fibroid tissue will be histologically investigated to assess vascular density and histological composition. A small part of the removed tissue will be kept apart for this purpose. Direct and indirect medical and non-medical costs will be used to perform a cost utility analysis.

Also, patients that do not want to participate (no pre-treatment) will be asked to be included in the non-randomized control group:

Title: pre-treatment versus no pre-treatment prior to laparoscopic myomectomy: a non-randomized comparison.

Objectives: same objectives as main study (pre-treatment versus no-pre-treatment)

Methods: Eligible patients that are not willing to participate in the trial will not be pre-treated, or will be treated with the gold standard: GnRHa. Those patients that choose not to be pre-treated will be asked to participate in the untreated, not-randomized control group and will (after informed consent) follow the same study flow as the randomized patients. This way, pre-treatment in general can be compared to no pre-treatment.

Study description

Background summary

Rationale: Laparoscopic myomectomy is increasingly performed over laparotomic myomectomy, because of the many benefits for the patient in terms of pain, hospital stay and recovery. In order to increase the success rate of a laparoscopic procedure pre-treatment to decrease the volume might be beneficial. Gonadotropin-releasing hormone agonists (GnRHa) are used for this purpose with good results in terms of volume reduction, but sometimes resulting in loss of distinction of the right surgical planes. Ulipristal is a new pre-operative treatment option for symptomatic fibroids, which has demonstrated good results in terms of volume reduction. The effect on cleavage planes is unknown. This study is performed to evaluate if Ulipristal is as effective as GnRHa in terms of surgical outcome.
Objective: to investigate if Ulipristal is non-inferior to GnRH in terms of intra-operative blood-loss (primary outcome), surgical time, surgical ease, complications, quality of life and costs.

Study objective

Objective: to investigate if Ulipristal is non-inferior to GnRH in terms of intra-operative blood-loss (primary outcome), surgical time, surgical ease,

complications, quality of life and costs.

Study design

Study design: Double blind randomized controlled multi-center trial.

Intervention

Intervention: Three months of Ulipristal 5 mg once daily combined with a saline injection (produced as placebo of Leuproreline) or (comparison)a single 11.25 mg Leuproreline injection with placebo tablets (once daily) .

Study burden and risks

Both Ulipristal and GnRHa have been registered for this indication. Safety has been tested and no specific risks apply.

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

Women visiting the gynecological outpatient department with symptomatic fibroids will be screened for eligibility. In order to be eligible to participate in this trial, a subject must meet all of the following criteria:
* provide written consent prior to any study related procedures
* pre-menopausal
* a planned resection of a maximum of 2 FIGO (PALM-COEIN classification) type 3, 4, 5, 6 or 2-5 fibroids of >5 cm
* the(se) fibroid(s) should be between 5 and 12 cm (maximum diameter)
* other fibroids should be small (<2 cm), not clinically relevant, or not resectable (e.g. difficult position), or type 7 (any size)
* eligible for laparoscopic myomectomy

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this trial:
* pregnancy
* (suspicion of) malignancy
* any type 0-2 fibroids smaller than 5 cm
* more than 2 type 3-6 fibroids > 5 cm that need to be removed (except type 7 fibroids of any size)
* use of any hormonal agents and not willing to discontinue their use
* use of anticoagulants
* coagulopathy
* Use of NSAIDs impacting bleeding before surgery
* Contraindication to laparoscopy procedure or causes of complications (multiple laparotomies, frozen pelvis, severe endometriosis)
* allergy to leuprolide acetate/comparable nonapeptides or Ulipristal

Study design

Design

Study phase: 4

Study type:	Interventional
Intervention model:	Parallel
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-01-2015
Enrollment:	99
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Esmya
Generic name:	Ulipristal
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Lupron
Generic name:	Leuprolide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	01-10-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-12-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-11-2015

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-07-2017
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
EudraCT	EUCTR2014-002832-15-NL
CCMO	NL49916.029.14