

**Title:** Safety and efficacy of Womed Leaf™, a novel barrier film to prevent intrauterine adhesion formation after hysteroscopic myomectomy: The PREG1 clinical trial.

Weyers<sup>1</sup>, S.; Capmas<sup>2</sup>, P.; Huberlant<sup>3</sup>, S.; Dijkstra<sup>4</sup>, J.; Hooker<sup>5</sup>, A.B.; Hamerlynck<sup>1</sup>, T.; Debras<sup>2</sup>, E.; De Tayrac<sup>3</sup>, R.; Thurkow<sup>6</sup>, A.L.; Fernandez<sup>2</sup>, H.

<sup>1</sup> Women's Clinic, Ghent University Hospital, Department of Obstetrics and Gynaecology, Ghent, Belgium.

<sup>2</sup> Bicêtre hospital, Department of Obstetrics and Gynaecology, Le Kremlin Bicêtre, France.

<sup>3</sup> Nîmes University Hospital, Department of Gynecology and Obstetrics, Nîmes, France.

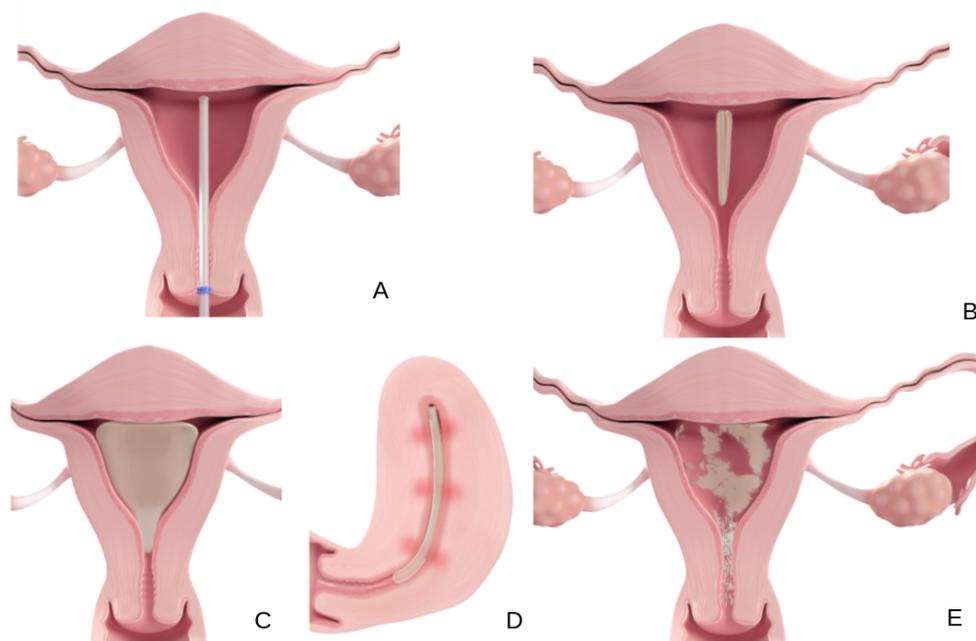
<sup>4</sup> Isala Zwolle, Department of Obstetrics and Gynaecology, Zwolle, The Netherlands.

<sup>5</sup> Zaans Medical Center, Department of Obstetrics and Gynaecology, Zaandam, the Netherlands.

<sup>6</sup> Bergman Clinics Amsterdam and Amsterdam University Medical Centres, Dept of Gynaecology, Amsterdam, the Netherlands.

**Aim:** Leiomyomata are the most common solid pelvic tumors in women. Hysteroscopic myomectomy is considered the gold standard for the management of women with types 0, 1 and 2 myomas suffering from bleeding disorders or subfertility. However, it carries the risk of postoperative intrauterine adhesion formation (IUA). The prevalence of IUAs following myomectomy continues to be high and varies significantly across the literature (7.5% - 45.5%). IUAs can lead to recurrent pregnancy loss, infertility, abnormal placentation, menstrual abnormalities, and pain.

The Womed Leaf™ intrauterine adhesion barrier film (Womed SAS, France) is a tri-block degradable polymer film (DPF) designed for insertion into the uterine cavity like an IUD at the end of a hysteroscopic procedure. The DPF absorbs fluid, expands to fill the entire cavity and stops the opposing uterine walls from coming in contact. After approximately one week, it hydrolytically degrades to be naturally discharged through the cervix (*Figure 1*). The objective of this first-in-human study was to evaluate the safety of this novel anti-adhesion barrier film and pilot its potential efficacy in preventing IUAs after hysteroscopic myomectomy.



*Figure 1: (A) Insertion of Womed Leaf into the cavity (B) Fluid absorption and self-deployment (C; D) The Womed Leaf fills the entire cavity (E) Hydrolytic degradation and natural discharge through the cervix.*

**Method:** PREG1 (trial registration number NCT04381728) is a prospective, multi-center, international, single arm, first-in-human clinical study. Six centers in France, Belgium and the Netherlands participated in the trial. Women over 40 years with no plans to conceive who qualified for hysteroscopic myomectomy, with at least one 10 millimeter type 0, 1 or 2 myoma were considered eligible for the study.

Women underwent transcervical resection of myoma (TCRM), and immediately after, a hysterometry was performed and the DPF was inserted, followed by a 2D / 3D endovaginal ultrasound to confirm the DPF deployment and position within the uterine cavity. All patients were contacted by phone 30 days after the TCRM to check for any potential adverse events. A follow-up hysteroscopy was scheduled 4-8 weeks after the TCRM in order to assess for presence of postoperative IUAs or DPF remnants.

**Results:** Between November 2019 and January 2021, 23 patients were enrolled into the study. The device was successfully introduced through the cervix with the loaded film and withdrawn empty following its intrauterine release on first attempt in all cases. The duration of DPF insertion was < 2 min in all cases and the procedure was rated as “easy” by all operators. The DPF was visible just after release in the uterine cavity using an endovaginal 2D or a 3D ultrasound in 22/23 women (96%).

There were no adverse incidents attributable to the DPF. Of the 23 women, 13 noticed the discharge of the DPF. Median time interval between the surgery and the discharge of the DPF was 6 days. Discharge duration was reported to last more than 1 day in 9/13. No residual DPF was found in the uterine cavity on second look hysteroscopy in any of the patients. On second look hysteroscopy, 20 of the 23 women (87%) had no IUAs.

**Conclusion:** Womed Leaf<sup>TM</sup>, the first mechanical barrier specifically designed to prevent IUA up to one week after hysteroscopic surgery, is a novel, safe, easy to apply and acceptable device for intrauterine adhesion prevention with very promising initial efficacy data.