

To be read carefully and returned signed by each new physician

The UTerine IMMune PROfiling (UTIMPRO test) increases pregnancy rates through personalized care (40-50% increase in birth rate, following application of the proposed treatments, at the next embryo transfer following the test). It is proposed for women experiencing, one, or both of the following:

- Embryo implantation failures (no implantation despite the transfer of several embryos of good quality)
- Repeated unexplained miscarriages (more than 3 miscarriages)

The purpose of this test is to document the immune environment of the uterus during the receptive period of the cycle (i.e. when the endometrium is susceptible to allow the implantation of an embryo, or *the implantation window* during mid luteal phase). This assessment is based on the diagnosis of a local immune imbalance which may interfere with the embryo implantation. The identification of the immunological mechanisms involved is based on the quantification by molecular biology of endometrial biomarkers (specific cytokines and modulators) regulating uterine immune cells. Given these data, you may consider to modulate and personalize your patient's next treatment to counter the potential identified local immune imbalance.

We recommend performing the biopsy on a mock cycle with estrogen and progesterone intake. The patient needs at least 10 days of estrogen alone before introducing the progesterone. Also, the biopsy should be done one week after the introduction of the progesterone (we accepted between 6 to 9 days after Pg). If you choose to carry out the sample on a natural cycle or with simple stimulation (FSH), the biopsy should be performed 8 to 11 days after LH surge or 9 to 12 days after the injection of ovitrelle while monitoring the luteal phase by dosing the progesterone ($\geq 8\text{ng / ml}$ 48 hours before the biopsy). In the event of a biopsy performed on a natural cycle, please ask the patient to notify us in case her period arrives within less than 4 days after the biopsy.

We recommend performing the biopsy with a full bladder in order to facilitate the passage of the pipelle. It is also important for any biopsy to be performed in conjunction with an ultrasound scan to measure the thickness of the endometrium, which must be at least 7 mm.

If the endometrial thickness is less than 7 mm, the biopsy must be cancelled and treatment for endometrial proliferation must be prescribed beforehand.

Once the biopsy has been performed (see instructions on the back), it must be placed quickly in the RNAlater tube provided and sent by post on the same day (if possible, otherwise place the biopsy in the refrigerator until it is sent):

We cannot proceed biopsies from patients whom serologies are positive for HIV, hepatitis B (Ag HBs, Ac HBc and Ac HBs) and hepatitis C. Cost of immune uterine profiling is 650 euros for European countries (costs for non-European countries or for control therapeutics biopsies are available our website: <https://matricelabinove.com/en/our-solution/>). Upon receipt of your patient's sample, and only after making sure that the RNA extraction is successfully done, we will contact the patient via e-mail to send the invoice. Then we will proceed to the real time PCR. **Results will be sent by email under 3 weeks** from the date of the biopsy receipt (except during the periods of laboratory closure or the health crisis). We will detail the immune mechanism if a deregulation is diagnosed as well as the options of personalization to counteract the deleterious disequilibrium. **The next IVF attempt can be considered between 2** (counting the time needed to receive the results and, in some cases, any treatments to be carried out before IVF) **and 6 months after the biopsy.**

Depending on the results, we may suggest a **therapeutic assessment** (a new biopsy with the therapeutic suggestions from the initial biopsy) in order to check the effectiveness of the treatment. **This new biopsy should be performed between 2 and 6 months after the first one, before transfer** (or in the event of pregnancy failure following transfer). In the event of a miscarriage or termination of pregnancy after the initial test, we recommend repeating this initial test rather than a test under therapeutics suggestions.

You can visit our website for further explanation: <http://www.matricelabinove.com/> or our facebook or instagram pages for news.

I, the undersigned Dr., certify that I have read and understood the conditions for performing and sending the biopsy as indicated on this document and the doctor's instructions.

Date : Signature :