

## INNOVATIVE APPROACH TO RECURRENT VAGINITIS

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**Introduction:** The vagina environment is dynamic and is influenced by several factors that can change the microbiota. As consequence, vaginal infections, as bacterial vaginosis (BV), anaerobic vaginitis (AV), vulvovaginal candidiasis (VVC) can develop. Furthermore, a link between inflammatory bowel disease (IBD) and vaginal infections has been observed. Despite the high cure rates achieved with standard drug therapy, very high recurrence rates (about 50%) associated to the normal protective vaginal flora reduction and some relevant treatment side effects (including antibiotic resistance) have been reported. This led researchers to investigate alternative remedies, as the use of Lactobacilli based on their key role in maintaining the balance in vaginal ecosystem aimed to limit the use of pharmacological therapy. This work presents a plan for developing "non-pharmacological clinical study" that will implement standardised "GCP-like procedures" in order to increase the scientific reliability of results.

### Method:

1. The probiotics Lactobacilli and phytoactive substances with anti-inflammatory, antifungal/antibacterial and lenitive action to be used in innovative products have been identified through a bibliographic research;
2. A well-designed clinical study with adequate population, sample size, follow-up and monitoring has been planned to test this non-pharmacological innovative integrated approach for recurrent vaginitis. The study will be conducted implementing "GCP-like procedures", including regular monitoring. Any causal relationship between possible adverse events/undesirable effects and investigational products or research procedures will be evaluated. The informed consent process will be conducted in accordance with the ethical principles originated from the Helsinki Declaration, Reg. (EC) 2016/679(GDPR), CIOMS-WHO Ethical Guidelines (2016), the Additional Protocol to the Oviedo Convention (2005), CE Recommendation Rec (2006)4.

**Results:** The following substances have been identified and included in innovative products:

- Oral food mixture including Beta(1,3)-(1,6)-beta-D-Glucan, L. rhamnosus and L. paracasei;
- Two cosmetic vaginal gels, an antimicrobial lenitive vaginal gel containing thyme essential oil, sage essential oil and calendula extract, and an intimate vaginal gel with L. plantarum;
- Functionalised pad with glycolic extracts (thyme, sage and calendula).

A single-centre, prospective, randomised, placebo-controlled, single blind, 2-parallel arms, non-pharmacological clinical study has been designed. The primary objective is to evaluate the efficacy of the proposed integrated approach to restore and maintain a lactobacilli-dominated vaginal microbiome after 2months of use. The positive outcome is the increase of vaginal Lactobacillus counts in the vaginal microbiome. 100 women of reproductive age with BV, AV, or VVC will be enrolled and randomised (1:1). The overall study duration is 6months (2-month subjects' enrolment; 2-month IPs use; 2-month subject observation). Secondary objectives of the study include the evaluation of clinical symptoms after 2and 4months, the reduction of the BV, AV, VVC recurrence rates, the collection of possible undesirable effects/adverse events, the evaluation of vaginal environment based on Amsel criteria and of the faecal microbiome in subjects with remote history of IBD. The study has been submitted to the competent Ethics Committee.

**Discussion and conclusion:** The present clinical study will allow to collect efficacy data on Lactobacilli used in combined approach to restore both vaginal flora and intestinal flora associated to decrease of BV, AV, VVC relapses, increasing the knowledge on their use, and to develop proper and well-studied formulations with adequate number of bacteria, viability, and administration schedule.

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