# HPV infection clearance with glucan and probiotics

Submission date	Recruitment status	Prospectively registered
10/08/2022	No longer recruiting	Protocol
Registration date	Overall study status	Statistical analysis plan
11/09/2022	Completed	Results
Last Edited	Condition category	Individual participant data
30/08/2022	Infections and Infestations	Record updated in last year

#### Plain English summary of protocol

Background and study aims

The aim of this study is to measure the effectiveness and safety of local treatment with a vaginal gel based on carboxy-methyl-beta-glucan in polycarbophil plus an oral probiotic containing an L. rhamnosus TOM 22.8 strain on genital human papillomavirus (HPV) infections. HPV is estimated to infect up to 80% of sexually active women by age 50 years. Although most HPV infections resolve over time, persistent infection can cause precancerous lesions and eventually lead to invasive cancer, mainly at the cervix. Nevertheless, HPV presence alone is not enough for cancer formation and local immunity in conjunction with low numbers of vaginal lactobacilli (bacteria) seem to be pivotal in cancer development. Beta-glucans have several roles in the human body such as increasing resistance to infectious diseases and a modulator action for the immune system. Probiotics have been studied in the context of HPV with study outcomes aimed at enhanced genital viral clearance

Who can participate?

Patients with low-grade pap smear anomalies or with a positive HPV DNA test

What does the study involve?

Participants are randomly allocated into four groups:

Group 1. Treatment with one capsule a day for 10 days per month for 3 months containing Lactobacillus rhamnosus TOM 22.8 10 x 10e9 U.F.C and vaginal gel-based carboxy-methyl-beta-glucan one application/day for 20 days per month for 3 months

Group 2. Treatment with one capsule a day for 10 days per month for 3 months containing Lactobacillus rhamnosus TOM 22.8 10 x 10e9 U.F.C., immediately after the end of each menstrual period

Group 3. Treatment with vaginal gel-based carboxy-methyl-beta-glucan 1 application/day for 20 days per month for 3 months, immediately after the end of each menstrual period Group 4: Untreated women, as the control group

On study day 180 (follow-up visit) the Pap test, HPV-DNA test, colposcopy and vaginal samples are taken to evaluate bacteria. In Groups 1, 2 and 3 compliance, treatment security, and allergic reactions will be also evaluated.

What are the possible benefits and risks of participating? The treatment may resolve pap smear anomalies and eliminate HPV infection. The researchers are not aware of adverse events related to the treatment.

Where is the study run from?
Ospedale dei Bambini Vittore Buzzi (Italy)

When is the study starting and how long is it expected to run for? June 2022 to June 2023

Who is funding the study? Investigator initiated and funded

Who is the main contact?

Prof. Filippo Murina, filippo.murina@unimi.it

## Contact information

#### Type(s)

Principal investigator

#### Contact name

Prof Ilippo Murina

#### Contact details

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## Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

SDSM-2021-01.1

# Study information

#### Scientific Title

Effects on cervical high-risk human papillomavirus clearance in patients undergoing treatment with vaginal gel based on carboxy-methyl-beta-glucan in polycarbophil plus an oral probiotic containing L. rhamnosus TOM 22.8 strain: a randomized controlled trial

#### Acronym

**HPGC** 

#### **Study objectives**

The aim of this study is to prospectively document the efficacy and safety of local therapy with a vaginal gel based on carboxy-methyl-beta-glucan in polycarbophil plus an oral probiotic containing L. rhamnosus TOM 22.8 strain on genital high-risk human papillomavirus (HR-HPV) clearance and low-grade squamous intraepithelial lesion (LSIL)/cervical intraepithelial neoplasia (CIN) 1 regression.

#### Ethics approval required

Old ethics approval format

#### Ethics approval(s)

Not provided at time of registration

#### Study design

Single-center randomized controlled trial

#### Primary study design

Interventional

#### Study type(s)

Treatment

#### Health condition(s) or problem(s) studied

**HPV** infection

#### **Interventions**

Patient recruitment: PAP smears with mild anomalies (atypical squamous cells of undetermined significance [ASCUS] or LSIL) and/or a cervical biopsy-confirmed CIN 1, and a positive HPV DNA test. HPV infection will be detected using polymerase chain reaction (PCR) amplification of the viral DNA, followed by dot blot hybridization. At time zero, a vaginal sample will be obtained through a rubbed swab against the vaginal wall finalized to evaluate bacterial community composition by sequencing the 16S rRNA genes amplified from total genomic DNA isolated from the samples.

Randomization is determined by a computer-generated number list (MedCalc Version 20.110). The study population will be randomized into four groups:

Group 1. Treatment with one capsule a day for 10 days per month for 3 months containing Lactobacillus rhamnosus TOM 22.8 10 x 10e9 U.F.C and vaginal gel-based carboxy-methyl-betaglucan one application/day for 20 days per month for 3 months. The protocol will start immediately after the end of each menstrual period

Group 2. Treatment with one capsule a day for 10 days per month for 3 months containing Lactobacillus rhamnosus TOM 22.8 10 x 10e9 U.F.C., immediately after the end of each menstrual period

Group 3. Treatment with vaginal gel-based carboxy-methyl-beta-glucan 1 application/day for 20 days per month for 3 months, immediately after the end of each menstrual period Group 4: Untreated women, as the control group

On study day 180 (follow-up visit) the Pap test, HPV-DNA test, colposcopy and vaginal sample to evaluate bacterial community composition by sequencing the 16S rRNA genes will be repeated. In Groups 1, 2 and 3 compliance, treatment security, and allergic reactions will be also evaluated.

#### Intervention Type

Supplement

#### Primary outcome(s)

HR-HPV clearance measured using PCR at 6 months

#### Key secondary outcome(s))

LSIL/CIN 1 regression measured using Pap smear/histology at 6 months

#### Completion date

30/06/2023

# **Eligibility**

#### Key inclusion criteria

- 1. Women aged 30-45 years
- 2. Persistent positive cytological LSIL and/or histological CIN 1 and/or HPV HR test for at least 12 months
- 3. Absence of contraindications to the proposed therapies
- 4. Read and signed informed consent

#### Participant type(s)

**Patient** 

## Healthy volunteers allowed

No

#### Age group

Adult

#### Sex

Female

#### Key exclusion criteria

- 1. Active vulvovaginal infections at the time of their gynaecological examination
- 2. Genital bleeding of unknown origin
- 3. Pregnancy
- 4. Menopause (absence of menstruation for 12 months)
- 5. Diagnosis of or under therapy for previous CIN2+ lesions
- 6. Immune-depressed, or with infections caused by human immunodeficiency virus (HIV-positive)
- 7. Patients concomitantly included in different interventional clinical trials
- 8. Unwillingness to provide informed consent to the trial

#### Date of first enrolment

01/06/2022

#### Date of final enrolment

31/12/2022

## Locations

#### Countries of recruitment

Italy

### Study participating centre Ospedale dei Bambini Vittore Buzzi

Lower Genital Tract Unit
Obst. and Gyn Dept.
Via Castelvetro 22
Milano
Italy
20122

# Sponsor information

#### Organisation

Ospedale dei Bambini Vittore Buzzi

#### **ROR**

https://ror.org/044ycg712

# Funder(s)

#### Funder type

Other

#### **Funder Name**

Investigator initiated and funded

## **Results and Publications**

#### Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date

#### IPD sharing plan summary

Data sharing statement to be made available at a later date

**Study outputs** 

Output type Details Date created Date added Peer reviewed? Patient-facing?

Participant information sheet Participant information sheet 11/11/2025 No Yes