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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

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
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

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

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-beta-glucan 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 measure
HR-HPV clearance measured using PCR at 6 months

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

Overall study start date
01/06/2022

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

Age group
Adult

Sex
Female

Target number of participants
80 patients total, 20 for each group

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

Sponsor details
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Sponsor type
Hospital/treatment centre

Website
https://ospedaledeibambini.it/noi-e-il-buzzi/

ROR
https://ror.org/044ycg712

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
The researchers plan to publish the study around September 2023.

Intention to publish date
01/09/2023

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