ISRCTN34437150 https://doi.org/10.1186/ISRCTN34437150

Impact of vaginal microbiome on HPV clearance and persistence in CIN2-CIN3 women

Submission date
31/01/2020

Recruitment status
No longer recruiting

Registration date
21/02/2020

Overall study status
Completed

Last Edited
01/12/2020

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims.
Persistent infection by a high-risk oncogenic (cancer-causing) type of Human Papillomaviruses (hrHPV) is related to precancerous lesions and invasive cervical cancer. Cervical cancer still remains one of the most frequent cancers in women worldwide.

hrHPV infection is necessary to cause cancer, but other additional factors are needed to be present too. Many factors have been proven to increase the oncogenic ability of hrHPV finally leading to the development of cancer. Among them, in recent years the composition of the vaginal microbiome has been suggested to have a critical role in cervical cancer development, but its role has not yet been made fully clear. Currently, there are no data on the potential importance of the vaginal microbiome in the recovery of patients after surgical removal of cervical cancer.

This study aims to assess if specific types of vaginal microbiota are linked to an increased or decreased possibility of recovery after surgical removal of HPV-related cervical cancer. In addition, the vaginal environment will be characterized, to understand if inflammation is an important factor in this process.

The results will be helpful in understanding if the vaginal microbiome can have a role in clearing HPV infection or in promoting its persistence. This could possibly pave the way to future treatments based on the use of specific bacteria to restore a protective vaginal microbiome and improving the outcomes of patients with, or at risk of, cervical cancer.

Who can participate?
Women aged 30 to 50 years, affected by CIN2-CIN3 cervical lesions

What does the study involve?
The study is only observational, as the only intervention is the surgical treatment of CIN lesion. No pharmacological or other kinds of additional treatment are planned.

What are the possible benefits and risks of participating?
Participating women will be analyzed for their vaginal microbiome and vaginal secretions, thus

providing a deeper knowledge of their situation and possible prognosis. Participants are not exposed to any risk.

Where is the study run from?
The gynecological center of the University Hospital of Ferrara (Italy)

When is the study starting and how long is it expected to run for?
April 2017 to February 2020

Who is funding the study?
No specific funds are used for this study. Each investigator will use his/her academic funds to run the study.

Who is the main contact?
Prof Elisabetta Caselli
csb@unife.it

Contact information

Type(s)
Scientific

Contact name
Prof Elisabetta Caselli

ORCID ID
http://orcid.org/0000-0001-6048-9141

Contact details
Section of Microbiology
Department of Chemical and Pharmaceutical Sciences
via Luigi Borsari 46
Ferrara
Italy
44121
+39 0532 455387
elisabetta.caselli@unife.it

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
03

Study information

Scientific Title
Vaginal microbiota and chemokine microenvironment in women surgically treated for cervical intraepithelial neoplasia and their association with HPV clearance/persistence

Study objectives
The vaginal microbiome has been associated with HPV infection, but no data are available on its role in HPV clearance and persistence in women affected by cervical intraepithelial neoplasia lesions with surgical treatment. The aim of the study is to assess this aspect and simultaneously evaluate also the vaginal chemokine profile with particular attention to the pro-inflammatory factors.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/07/2017, the Ethical Committee of the Province of Ferrara (Azienda Ospedaliero, Universitaria di Ferrara, Via Aldo Moro 8, Ferrara 44124; +39 0532 236896, +39 0532 455727; ulrich.wienand@unife.it) ref: 170394

Study design
Longitudinal, observational, cohort, single-centre, prospective study.

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Screening

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

Health condition(s) or problem(s) studied
cervical intraepithelial neoplasia, HPV, CIN2, CIN3

Interventions
The study is only observational, as the surgical intervention to remove the CIN lesion is part of the planned clinical treatment for such type of disease.

The study focuses on the characterization of vaginal microbiome and vaginal microenvironment in patients affected by CIN2-CIN3 cervical lesions and undergoing surgical treatment to remove lesions.

Each patient undergoing the surgical treatment of CIN2 or CIN3 lesion, and signing informed consent to participate in the study, will have their vaginal microbiome and vaginal cytokines characterized at baseline (the day of surgical treatment) and after 6 months (follow-up). They will also be assessed by a clinician at baseline and 6 months.

The vaginal microbiome is characterized by molecular biology, using a quantitative real-time PCR microarray detecting and quantifying simultaneously 90 microbial species (including bacteria, mycetes, and protozoa) typically found in vaginosis.

The vaginal environment is characterized by analyzing the presence and concentration of twelve pro-inflammatory cytokines, by ELISA assays. The analyzed cytokines are: IL1α, IL1β, IL2, IL4, IL6, IL8, IL10, IL12, IL17α, IFNγ, and TNFα.

Cervicovaginal samples are collected by sterile rayon swabs put in 0.4 ml of sterile phosphate-buffered saline (PBS) in a 1.5 ml microtube. Collected samples are immediately refrigerated and transported to the laboratory for processing within 3 hours. Total DNA is extracted from the cervicovaginal swab samples upon arrival at the laboratory (within 3 hours from the collection). Extracted DNA is quantified by spectrophotometric reading and checked for amplifiability by a panbacterial PCR and a PCR amplifying a human house-keeping gene (beta-actin)

Vaginal secretions are collected by washings the vaginal cavity with 5 ml of sterile physiological solution. The collected samples are distributed in sterile 1.5 ml microtubes, immediately refrigerated and then frozen at -80°C until use.

Intervention Type
Procedure/Surgery

Primary outcome measure
The role of the vaginal microbiome in HPV clearance and persistence in CIN patients measured by quantitative real-time PCR microarray of DNA extracted from cervicovaginal swabs taken at baseline and 6 months

Secondary outcome measures
1. Presence of pro-inflammatory cytokines in the vaginal microbiome measured by ELISA assays of vaginal secretions collected at baseline and 6 months
2. Concentration of pro-inflammatory cytokines in the vaginal microbiome measured by analysis of ELISA assays of vaginal secretions collected at baseline and 6 months

Overall study start date
01/04/2017

Completion date
29/02/2020

Eligibility

Key inclusion criteria
1. High risk HPV-positive patients
2. CIN2 or CIN3 cervical lesions
3. Planned removal of cervical lesions by surgical intervention

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
100

Total final enrolment
85

Key exclusion criteria
1. Pregnancy
2. Lactation
3. Concomitant infections
4. Concomitant neoplasias

Date of first enrolment
01/01/2019

Date of final enrolment
31/01/2020

Locations

Countries of recruitment
Italy

Study participating centre
University of Ferrara
via Luigi Borsari 46
Ferrara
Italy
44121

Sponsor information

Organisation
University of Ferrara

Sponsor details

via Luigi Borsari 46
Ferrara
Italy
44121
+39 0532 455387
csb@unife.it

Sponsor type
University/education

Website
http://www.unife.it/

ROR
https://ror.org/041zkgm14

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
Investigators plan to publish results as soon as possible, once the enrollment of study participants is complete.

Intention to publish date
31/07/2020

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication

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?
Results article	results	05/11/2020	01/12/2020	Yes	No