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The development of technologies increasing diagnosis and treatment efficiency of the cervix diseases associated with human papillomavirus (HPV)

Submission date
03/07/2023

Recruitment status
No longer recruiting

Registration date
11/07/2023

Overall study status
Completed

Last Edited
03/10/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Cervical cancer (CC) is a common type of cancer affecting the female reproductive system. Cervical intraepithelial neoplasia (CIN) is a precancerous condition that can lead to CC. Women with CIN have a 20 times higher risk of developing CC compared to healthy women. It is crucial to treat CIN in its early stages to prevent its progression to invasive CC.
Human papillomavirus (HPV) is a group of viruses that are widespread worldwide. Oncogenic HPV can persist in the body and evade the immune system, leading to sequential carcinogenesis from infection to invasive cancer. HPV infection is detected in over 99.7% of CC cases and is considered the main risk factor for CIN.
Traditional treatments for CC include surgery, radiation, and chemotherapy, but these methods can have side effects and impact fertility. Therefore, there is a need for effective alternative treatments for CIN and cervical HPV that do not compromise fertility.
Photodynamic therapy (PDT) is a promising approach to prevent the recurrence of HPV-associated cervical lesions. PDT involves using photosensitizers (PS), which accumulate in affected tissue. When these PS interact with light of a specific wavelength, they initiate photophysical processes that damage or destroy the affected area. PDT consists of two stages: administering the PS and directing local light irradiation. The success of PDT depends on oxygen-induced activation of the PS, proper use of visible light, and the appropriate choice of PS. These factors lead to the formation of free radicals, such as singlet oxygen, which cause local photooxidation, cell damage, and destruction.
To enhance the effectiveness of HPV-associated infection treatment, a combination of local PDT and systemic photosensitivity during intravenous laser blood irradiation (SPILBI) is proposed. This program aims to develop an innovative technology that improves the diagnosis and treatment of background and precancerous cervical lesions associated with HPV.
The research hypothesis will test the cumulative effect of three components of laser technology with photosensitivity: fluorescent diagnostics using PS, evaluation of PS "burnout" during local

PDT, and SPILBI. Genetic and immunological features of the innate immune response, along with viral and bacterial load indicators, liquid cytology, and immunocytochemical assessment, will be considered to personalize the approach to PDT based on the heterogeneity of the disease.

Who can participate?
Adult women aged 18 - 45 years with CIN and HPV

What does the study involve?
The main group will undergo local and systemic PDT without antiviral therapy. The control group will undergo antiviral therapy using geneferon and valaciclovir but without PDT.

What are the possible benefits and risks of participating?
Potential inconveniences and risks associated with the study do not exceed the inconveniences and risks during PDT and the administered physiological dose of the Photolon photosensitizer. Participation in a study may require longer and more frequent visits to the doctor than regular appointments. Control examinations after photodynamic therapy will be carried out after 1, 3, 6 and 12 months. In case of poor-quality performance, the risks are as follows: during PDT, pain of varying severity (from a burning sensation to sharp pains) in the irradiation area is possible and can persist from several hours to 1 day, fever is rarely observed to subfebrile figures on the 2nd day after the procedure, which may be a consequence of the development of aseptic inflammation after intracavitary PDT. Allergic reactions are possible. Within 1-2 months after the administration of PS, phototoxic skin reactions are possible when exposed to sunlight. With an increase in temperature to subfebrile figures, a transient increase in blood pressure, special treatment is not required, and activities continue in accordance with the developed program. In general, the complication rate does not exceed 5%.

Where is the study run from?
Ministry of Science and Higher Education of the Republic of Kazakhstan

When is the study starting and how long is it expected to run for?
August 2022 to December 2024

Who is funding the study?
Ministry of Science and Higher Education of the Republic of Kazakhstan

Who is the main contact?
Shanazarov Nasrulla Abdullayevich, Shanazarov@bmc.mcudp.kz

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
The development of innovative technologies increasing diagnosis and treatment efficiency of the cervix background and precancerous diseases associated with HPV

Acronym
PDT-HPV

Study objectives
The effectiveness and safety of using a combination of local and systemic photodynamic therapy (PDT) for the diagnosis and treatment of the Human Papilloma Virus (HPV)-associated Cervical intraepithelial neoplasia (CIN) in Kazakh women of reproductive age, taking into account their genotypic and immunological characteristics.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 09/08/2022, Local Commission on Bioethics of the Medical Center Hospital of the President's Affairs Administration of the Republic of Kazakhstan (80, Mangilik El Street, Astana, 010000, Kazakhstan; +7 87172708102; sibagatova@bmc.mcudp.kz), ref: Avdeyev@bmc.mcudp.kz

Study design
Single-center interventional non-randomized controlled trial

Primary study design
Interventional

Study type(s)
Diagnostic, Treatment

Health condition(s) or problem(s) studied
HPV-associated cervical intraepithelial neoplasia

Interventions
The study aims to recruit two cohorts of patients with established HPV and cervical intraepithelial neoplasia (CIN). The main group will consist of 150 participants from the hospital, who will undergo local and systemic photodynamic therapy (PDT) without antiviral therapy. The control group will include 50 women who will undergo antiviral therapy using geneferon and valaciclovir, but without PDT.

The procedure begins by administering the photosensitizer "Photolon" intravenously after dilution with saline. After 2-3 hours, the systemic photosensitivity during intravenous laser blood irradiation (SPILBI) procedure is performed. This involves irradiating the blood with light through an optical fiber inserted into a vein using the LAMI-Helios laser device from Russia. The SPILBI procedure lasts approximately 30-50 minutes. The photosensitizer accumulates in tumor tissue more than healthy tissues and organs, and when irradiated with light, it induces a photochemical reaction that destroys the cancer cells.

Following the SPILBI procedure, a local PDT is performed. The patient is positioned on a gynecological chair, and under the guidance of a colposcope, fluorescent diagnostics is performed to identify all the pathological areas of the cervical epithelium accurately. Special light guides and thin diffusers are used to deliver light from a laser with a wavelength between 395-405 nm to the affected epithelium. This makes the pathological areas visible and accessible for PDT.

Intervention Type
Mixed

Primary outcome(s)
1. Differential detection and quantitative determination of HPV, as well as a test for ureaplasmosis, mycoplasmosis, candidiasis are performed using the Real-time CFX96 Touch amplifier (USA) 3, 6, 12 months after PDT

Key secondary outcome(s))
1. Full blood count is measured using the hematology analyzer Sysmex XN-3000 (Japan) at the 5th day and 3, 6, 12 months after PDT.
2. CD3, CD4, CD8, CD19, CD16, CD 56 are measured using the flow cytometer BD FACSCanto II Becton Dickinson (USA) at the 5th day and 3, 6, 12 months after PDT.
3. Interleukin 1, interleukin 6, and tumor necrosis factor are measured using the enzyme immunoassay at the Freedom EVOlyzer (Tecan, Austria) at the 5th day and 3, 6, 12 months after PDT.
4. To determine cervical intraepithelial neoplasia (CIN) colposcopy is performed 3, 6, 12 months after PDT.

Completion date
20/12/2024

Eligibility

Key inclusion criteria

1. Female
2. Age 18 - 45 years old
3. Established diagnosis of CIN
4. Positive PCR result for HPV
5. Lack of surgical treatment of CIN / absence of conization of the cervix
6. Kazakh nationality

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
45 years

Sex
Female

Key exclusion criteria
1. Male
2. Age under 18 and over 45 years
3. Surgical treatment of CIN / conization of the cervix
4. Persons mentally or legally incompetent, which prevents obtaining informed consent
5. Pregnant or lactating women
6. Acute gonococcal and non-gonococcal infections of the urethra and lower reproductive tract
7. Severe and decompensated diseases of the liver and kidneys, cardiovascular system
8. Autoimmune diseases
9. Oncological diseases
10. Porphyria and other photoallergic conditions
11. Taking anticoagulants

Date of first enrolment
03/03/2023

Date of final enrolment
30/09/2023

Locations

Countries of recruitment
Kazakhstan

Study participating centre
RSE “Medical Center Hospital of the President’s Affairs Administration of the Republic of Kazakhstan” on REU
80, Mangilik El Street
Astana
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Sponsor information

Organisation
Ministry of Science and Higher Education of the Republic of Kazakhstan

Funder(s)

Funder type
Government

Funder Name
Ministry of Science and Higher Education of the Republic of Kazakhstan

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Shanazarov Nasrulla Abdullayevich (Shanazarov@bmc.mcudp.kz)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other unpublished results			03/10/2025	No	No
Participant information sheet			05/07/2023	No	Yes
Participant information sheet			05/07/2023	No	Yes
Participant information sheet			05/07/2023	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes