Clinical Trial Protocol
Iranian Registry of Clinical Trials

17 Sep 2026

Phase II Clinical Trial of Safety, Immunogenicity, and Mucosal Immunotherapy of Recombinant Lactococcus lactis Expressing Human Papillomavirus Type 16 E6/E7 Oncoprotein Vaccine (KMTLL16E6/7) in Women Suffering From Cervical Intraepithelial Neoplasia (CIN) Grade 2/3

Protocol summary

Study aim

The primary goal of this study is to assess the safety and immunogenicity of oral administration of KMTLL16E6/7 vaccine to patients with CIN2/3 and also determine the recommended human dose to obtain the optimal efficacy. The secondary goal of this study is an in-depth assessment of the efficacy of KMTLL16E6/7 vaccine in induction of TH1 immune responses against E7 and E6 oncogenes, cytological regression of CIN2/3, and clearance of HPV-16 genome.

Design

Two hundred and twenty Iranian women aged 18 to 59 years old with Cervical Intraepithelial neoplasia Grade 2/3 will be vaccinated at the Keyvan Virology Specialty Laboratory (KVSL). Upon Enrollment, Written Consent will be Obtained From Each Participant or Her Legal Guardian.

Settings and conduct

After obtaining the informed consent form of the women with cervical intraepithelial neoplasia in Keyvan Virology Specialty Laboratory, detailed information on how to use vaccines KMTLL16E6/7 as well as when and how to do required experiments after using the mentioned vaccine will be given to them.

Participants/Inclusion and exclusion criteria

1- Women Have PCR positive test for Papilloma Virus Infection; 2- Women Don't be Pregnant; 3- Women in Pap smear Test Have Abnormal Conditions; 4- Failure to Complete a Course of Treatment by Individuals Will Result in Their Exclusion from Study.

Intervention groups

In This Study, There Are Six Target Groups That All Groups Are Identical in Terms of disease, But Differ in Terms of Drug Use. This Will be Given to Three Groups (Test Groups) of the E7 and E6 Vaccine and Will be Given to the Following Three (Control Groups) Groups of Placebo.

Main outcome variables

Evaluation of Safety, Immunogenicity, and Mucosal Immunotherapy of KMTLL16E6/7 Vaccine in Women having Cervical Intraepithelial neoplasia

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20190504043464N2**
Registration date: **2020-02-07, 1398/11/18**
Registration timing: **registered_while_recruiting**

Last update: **2020-02-07, 1398/11/18**
Update count: **0**

Registration date

2020-02-07, 1398/11/18

Registrant information

Name

Sedigheh Taghinezhad Saroukalaei

Name of organization / entity

Country

Iran (Islamic Republic of)

Phone

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Email address

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2020-02-01, 1398/11/12

Expected recruitment end date
2020-08-01, 1399/05/11
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Phase II Clinical Trial of Safety, Immunogenicity, and Mucosal Immunotherapy of Recombinant Lactococcus lactis Expressing Human Papillomavirus Type 16 E6/E7 Oncoprotein Vaccine (KMTLL16E6/7) in Women Suffering From Cervical Intraepithelial Neoplasia (CIN) Grade 2/3

Public title
Phase II Clinical Trial of Safety, Immunogenicity, and Mucosal Immunotherapy of Recombinant Lactococcus lactis Expressing Human Papillomavirus Type 16 E6/E7 Oncoprotein Vaccine in Women having Cervical Intraepithelial Neoplasia (CIN)
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
The women must have the ability to understand the study requirements, sign the Informed Consent Form, and also understand all restrictions during the study. 18-59 years-old females who are diagnosed as CIN2/3 by histological examination and are infected with HPV-16 alone or HPV-16 plus other types have the eligibility to enter in the study Women shouldn't have other sexually transmitted diseases. Women shouldn't be pregnant before starting the study. Women shouldn't have other cancerous disease.
Exclusion criteria:
Patients who has a previous history of hypersensitivity to probiotic-content (food/drug or milk). Patients who are suspected to invasive cancers. Patients with the medical history of diseases that may endanger the safety of the participant. Patients with a history of allergic diseases or reactions that may be aggravated by any component of the vaccine in question. Patients who have plan to do surgery during the study. Patients who used antibacterial drugs in 14-28 days before the study. Patients who used any vaccine within 90 days prior to screening. Patients who have plan to participate in another clinical trial during the present trial study. Patients who have autoimmune diseases or immunosuppressive disease. Patients with positive results of the HIV-1/2 antibodies, HCV antibody, HSV antibody, and HBsAg on screening process will be excluded from the study.
Age
From **18 years** old to **59 years** old
Gender
Female

Phase
2
Groups that have been masked

- Participant

Sample size
Target sample size: **220**
Randomization (investigator's opinion)
Randomized
Randomization description
Eligible candidates were divided into six clinical groups with a ratio of 2:1 by using Randomizer Software (version 3.0) to receive 4 periods of oral vaccines of E6 or E7 or placebo at weeks 1, 2, 4 and 8 . Each dose of the vaccine was administrated orally, once each morning, and for five days each treatment week. Subjects will be followed for 1 year after each intervention.
Blinding (investigator's opinion)
Single blinded
Blinding description
In this study, women who suffering from cervical intraepithelial neoplasia grade 2/3 are divided into six groups. In this phase, all groups are treated and simultaneously given to three groups of vaccines and given to the other three groups of placebo.
Placebo
Used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Iran University of Medical Siences
Street address
Iran University of Medical Sciences, Shahid Hemmat Highway, Tehran
City
Tehran
Province
Tehran
Postal code
1449614535
Approval date
2016-12-20, 1395/09/30
Ethics committee reference number
1395.95-04-30-29914

Health conditions studied

1

Description of health condition studied
Genital Wart
ICD-10 code
A63.0
ICD-10 code description
Anogenital (venereal) warts

Primary outcomes

1

Description
Measurement the level of Th1 type IFN-γ and antigen-specific CTLs secretion in PBMC and vaginal fluids
Timepoint
At the Beginning of the Study (on day 0 before the initial vaccination), at day 60 After Taking the Vaccine., and at months 1, 6, and 12 after the last vaccination.
Method of measurement
ELISPOT KITS

2

Description
Determining the presence/absence of HPV-16 in cervical fluids
Timepoint
At the Beginning of the Study (on day 0 before the initial vaccination), at day 60 after taking the vaccine, and at months 1, 6, and 12 after the last vaccination.
Method of measurement
PCR and INNO-LiPA Techniques

3

Description
Examination of cervix and vagina for evaluating and predicting the malignant and CIN status in treated women.
Timepoint
At the Beginning of the Study (on day 0 before the initial vaccination), at day 60 after taking the vaccine, and at months 1, 6, and 12 after the last vaccination.
Method of measurement
Colposcopy and Cervical Biopsy

Secondary outcomes

empty

Intervention groups

1

Description
Intervention group: Volunteers will receive four rounds of oral vaccine (1 mL) at weeks 1, 2, 4, and 8. Each dose of vaccine will be administered orally, once each morning after fasting for five days, each treatment week. If no side effects were detected in arms given the lower dose (1000000000 CFU/mL), the dose will be escalated to 5000000000 CFU/mL and 10000000000 CFU/mL.
Category
Treatment - Other

2

Description
Control groups will receive four rounds of placebo (1 mL) at weeks 1, 2, 4, and 8. Each dose of placebo will be administered orally, once each morning after fasting for five days, each treatment week. If no side effects were detected in arms given the lower dose (1000000000 CFU/mL), the dose will be escalated to 5000000000 CFU/mL and 10000000000 CFU/mL.
Category
Treatment - Other

Recruitment centers

1

Recruitment center
Name of recruitment center
Keyvan Virology Specialty Laboratory
Full name of responsible person
Hossein Keyvani
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
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Full name of responsible person
Dr. Abbas Motavalian
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Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Iran University of Medical Sciences
Proportion provided by this source

50

Public or private sector
Private

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin

Type of organization providing the funding
Academic

Person responsible for general inquiries

Contact

Name of organization / entity
Islamic Azad University

Full name of responsible person
Amir Hossein Mohseni

Position
Researcher

Latest degree
Ph.D.

Other areas of specialty/work
Microbiology

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Undecided - It is not yet known if there will be a plan to make this available

Study Protocol
Undecided - It is not yet known if there will be a plan to make this available

Statistical Analysis Plan
Undecided - It is not yet known if there will be a plan to make this available

Informed Consent Form
Undecided - It is not yet known if there will be a plan to make this available

Clinical Study Report
Undecided - It is not yet known if there will be a plan to make this available

Analytic Code
Undecided - It is not yet known if there will be a plan to make this available

Data Dictionary
Undecided - It is not yet known if there will be a plan to make this available