ISRCTN32729817 https://doi.org/10.1186/ISRCTN32729817

Human papillomavirus infection: a randomised controlled trial of Imiquimod cream (5%) versus Podophyllotoxin cream (0.15%), in combination with quadrivalent human papillomavirus or control vaccination in the treatment and prevention of recurrence of anogenital warts

Submission date
25/07/2014

Recruitment status
No longer recruiting

Registration date
25/07/2014

Overall study status
Completed

Last Edited
28/09/2020

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Genital warts are a very common sexually transmitted disease and are caused in over 90% of cases by human papillomavirus (HPV) types 6 or 11. Podophyllotoxin (as a cream or solution) and imiquimod cream are the most frequently used topical treatments for genital warts, but they have never been adequately compared to determine their relative effectiveness with respect to the clearance or recurrence rate. A vaccine is available to prevent HPV 6 and 11 (as well as HPV 16 and 18, the viruses that cause most cervical cancer), but it is not known whether it will increase the rate of clearance of genital warts if it is given at the same time as topical treatment, or whether it can prevent recurrences. The aim of this study is to find out whether imiquimod or podophyllotoxin is more effective at clearing and preventing recurrence of genital warts, and whether the addition of HPV vaccination provides additional benefits.

Who can participate?
Patients aged 18 or over with genital warts

What does the study involve?
Participants are randomly allocated to be treated with either imiquimod cream or podophyllotoxin cream, and to be treated with either a course of quadrivalent HPV vaccine (active against HPV types 6/11/16/18) or a placebo (dummy injection). This results in four treatment groups: imiquimod cream plus HPV vaccine; podophyllotoxin cream plus HPV vaccine; imiquimod cream plus placebo vaccine; and podophyllotoxin cream plus placebo vaccine. Successful treatment is defined as clearance of warts after 16 weeks and no relapse between 16 and 48 weeks. The study also compares the time taken for warts to be cleared with each treatment, the number of patients switching treatment because of non-response to treatment

or side-effects, and the patients' quality of life. An analysis is also conducted to compare the cost effectiveness of each treatment. Imiquimod is currently more expensive than podophyllotoxin (although the cost difference is expected to reduce). The economic benefit of HPV vaccination is also studied.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
University College London (UK)

When is the study starting and how long is it expected to run for?
June 2014 to March 2017

Who is funding the study?
Health Technology Assessment Programme (UK)

Who is the main contact?
Dr Macey Murray
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2013-002951-14

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
16857; HTA 11/129/187

Study information

Scientific Title
Human papillomavirus infection: a randomised controlled trial of Imiquimod cream (5%) versus Podophyllotoxin cream (0.15%), in combination with quadrivalent human papillomavirus or control vaccination in the treatment and prevention of recurrence of anogenital warts (HIPvac Trial)

Acronym
HIPvac

Study objectives
The HIPvac trial will address two questions regarding the management of patients with genital warts. The first is which of the two most frequently used creams used to treat warts, imiquimod or podophyllotoxin, is most effective at clearing genital warts, and preventing recurrence. The second is whether a course of human papillomavirus (HPV) vaccine started at the time of initiating topical treatment, increases the effectiveness of the cream in either clearing the warts or preventing recurrence. The HPV vaccine used is licensed for the prevention of infection caused by HPV 6 and 11 (which cause 90% genital warts) and HPV 16 and 18 (cause 70% cervical cancer). The vaccine is used in the national vaccination programme in the UK for girls aged 12-13; it is not licensed for the treatment of genital warts.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/11129187
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0007/94642/PRO-11-129-187.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
13/SC/0638; First MREC approval date 03/02/2014

Study design
Randomised; Interventional; Design type: Not specified, Treatment

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 contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Topic: Infectious diseases and microbiology; Subtopic: Infection (all Subtopics); Disease: Infectious diseases and microbiology

Interventions
The trial will follow participants for 48 weeks (6 visits). They will be randomly assigned to one of the creams (imiquimod 5% or podophyllotoxin 0.15%). Patients will know which cream they have been given as the creams have different dosing schedules. The creams will be used per standard care. The vaccine will be randomly assigned at the same time. Participants will receive either HPV vaccine (Gardasil) or placebo (saline injection). Patients will receive three doses of vaccine, the first at their baseline visit, then at week 8 and 24.

Intervention Type
Mixed

Primary outcome measure
Wart clearance within 16 weeks of starting treatment and remaining wart-free between 16 and 48 weeks

Secondary outcome measures
1. Proportion wart-free at the end of the assigned treatment course; Timepoint(s): 4 or 16 weeks
2. Proportion experiencing wart recurrence/relapse after complete wart clearance; Timepoint(s): Up to 48 weeks
3. Time from complete wart clearance to recurrence/relapse; Timepoint(s): Up to 48 weeks
4. Adverse events; Timepoint(s): As required
5. Health-related quality of life, as measured by the Area Under the Curve for EQ-5D; Timepoint (s): At all visits
6. Symptom scores; Timepoint(s): At all review of treatment visits
7. Total costs of treatment including prescribed agents and clinic visits; Timepoint(s): 48 weeks
8. Proportion wart-free at 16 weeks, with use of additional treatment as required; Timepoint(s): 16 weeks
9. Quantity of additional treatment required to achieve clearance by 16 weeks; Timepoint(s): 16 weeks
10. Proportion wart-free at 24 weeks; Timepoint(s): 24 weeks
11. Proportion wart-free at 24 weeks with use of additional treatment as required; Timepoint(s): 24 weeks
12. Qantitiy of additional treatment required to achieve clearance by 24 weeks; Timepoint(s): 24 weeks
13. Proportion experiencing wart recurrence/relapse at 48 weeks after wart clearance at 24 weeks; Timepoint(s): 24, 48 weeks
14. Proportion experiencing complete wart clearance; Timepoint(s): 48 weeks
15. Time to complete wart clearance; Timepoint(s): Point of wart clearance

Overall study start date
30/06/2014

Completion date
31/03/2017

Eligibility

Key inclusion criteria
1. Age 18 years or over
2. Males and females
3. First episode or repeat episode of anogenital warts diagnosed clinically
4. External anogenital warts considered, in the opinion of the investigator, to be suitable for self-administered topical wart treatment (patients with concurrent internal anogenital warts are still eligible to participate)
5. Able to provide informed consent to participate in the trial

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 1000; UK Sample Size: 1000

Total final enrolment
503

Key exclusion criteria
1. Previous wart treatment in the last 3 months
2. Previous quadrivalent HPV vaccine (previous bivalent HPV vaccine is not an exclusion criterion)
3. Previous intolerance to either of the topical treatments, vaccines or their constituents
4. Known HIV-positivity (HIV testing is not required for the trial)
5. Pregnancy or lactation (current, or planned in the next 6 months)
6. Women of child bearing potential not willing to use effective contraception for the duration and 30 days post completion of trial treatment: see above
7. Unable or unwilling to complete follow-up procedures
8. Lesion area greater than 4 cm2, requiring treatment under direct supervision of medical staff (in accordance with
podophyllotoxin cream Summary of Product Characteristics)
9. Patients who have had topical steroids applied to the target area, or systemic steroids or other immunosuppressive agents, within 1 month prior to randomisation
10. Patients enrolled in any other trial of an Investigational Medicinal Product, without the permission of the Chief Investigator
11. Any clinical condition which the investigator considers would make the patient unsuitable for the trial, including immunodeficiency conditions

Date of first enrolment
30/06/2014

Date of final enrolment

31/03/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University College London
London
United Kingdom
WC1E 6BT

Sponsor information

Organisation
University College London (UK)

Sponsor details
Gower Street
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Sponsor type
University/education

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)

NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
01/04/2020

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?
Basic results				No	No
Protocol article	protocol	06/11/2018		Yes	No
Results article	results	01/09/2020	28/09/2020	Yes	No
HRA research summary			28/06/2023	No	No