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Evaluation of a new self applied treatment for early stage pre cancerous disease of the cervix

Submission date	Recruitment status	[_] Prospectively registered
11/04/2014	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
29/05/2014	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
01/02/2016	Cancer	

Plain English summary of protocol

Background and study aims
Cancer of cervix is the second leading cause of cancer deaths in women worldwide. Global estimates suggest that there are 452,000 new cases and more than 270,000 deaths every year. The number of cervical cancer cases, along with HIV/AIDS, are of particular concern in developing countries, such as Kenya. Cervical cancer is the leading cause of cancer-related deaths among women in developing countries. It is the most common cancer of the female reproductive system in Kenya. We have shown in our previous research that the main active component of the drug Lopimune(CIPLA, India) Lopinavir, usually given as tablets to treat HIV infection may also be successful in treating human papilloma virus (HPV) infections.
The aim of this study is to test the safety/tolerability of vaginally delivered Lopimune soft-gel capsules as a treatment for HPV mediated cervical disease in HIV negative patients and to also determine their effectiveness.

Who can participate?
HIV negative women aged >18years attending Kenyatta National Hospital's Family Planning Clinic and Gynaecology Out-patient Clinics in Nairobi, positive for the presence of high risk HPV and have been found upon cytological screening to have cervical abnormality (dysplasia).

What does the study involve?
Participants will be randomly allocated to oine of two groups: either once daily or twice daily Lopimune (self applied as a pessary) for a period of 2 weeks.
The effects of these treatments will be analysed during follow-up which includes colposcopic examination, repeat smear and HPV testing followed by a final punch biopsy.

What are the possible benefits and risks of participating?
Benefits - All those undergoing the initial screening will benefit from: Free counselling and HIV testing; Prompt referral for HIV disease relevant treatment and long-term follow-up; HPV testing; Standard pap smear and liquid based cytology smear ; Sexually transmitted disease screening and treatment if needed; Full blood count; Urea and electrolytes; Liver function tests; Transport costs to and from clinic. Any women found to have invasive cervical cancer will receive immediate treatment paid for by the study. Those who go onto be enrolled into the study will also benefit from continued follow up until 3 months post Lopimune application and, if needed,

at the end of the 3 months further ongoing standard care treatment (loop excision).
Any potential risks from this study would be as a result of the effects of Lopimune exposure on the vaginal and cervical tissue (e.g. vaginitis, cervicitis, dryness, itching etc) and systemic side effects as documented for oral Lopinivir.

Where is the study run from?
The study will be carried out at Kenyatta National Hospital in Nairobi.
Manchester University, UK will be responsible for some aspects of the diagnostic work and all the scientific aspects, which require access to specialist equipment.

When is study starting and how long is it expected to run for?
From April 2013 to April 2014

Who is funding the study?
Cancer Research Trust Kenya and the Caring Cancer Trust UK.

Who is the main contact?
Dr Ian Hampson, Reader in Viral Oncology, ian.hampson@manchester.ac.uk
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Lopinavir as a Topical Treatment (LOTT) trial for HPV-related cervical dysplasia in HIV negative women

Acronym
The LOTT Trial

Study objectives
Topical application of Lopimune to the cervix will be well tolerated and lead to HPV clearance and lesion regression in women with cervical dysplasia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Kenyatta National Hospita Research Ethics Board, ref. KNH/ERC/R/9, P273/05/2011

Study design
Non-randomised Interventional Design type: Treatment

Primary study design
Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
HPV related pre cancerous lesions of the cervix

Interventions
The study will involve the screening of 600 - 800 women who will be given HIV, HPV and other STI screening. Approximately 30 women who are HIV negative, HPV positive and show evidence of high grade cervical dysplasia will be enrolled into the Lopimune treatment part of the trial.

As a result of the screening:
Any woman testing positive for HIV will be given appropriate counselling, treatment and ongoing follow up. These results will be available within 2 weeks. Women identified with STDs will be referred for appropriate treatment. Women identified with high risk HPV will be will be provided with further information and counselling. Women identified with invasive cervical cancer or cervical dysplasia will be sent for colposcopy. Immediate treatment will be given for those with invasive cancer.

Those women with cervical dysplasia will be offered enrolment into the Lopimune stage of the study. This will consist of 1 Lopimune capsule twice daily for 2 weeks. All women will be examined every 2 days for adverse reactions. At 1 month post treatment they will be given colposcopy and a repeat LBC and HPV test. At 3 months post treatment this will be as per 1 month follow up, but extended to include a punch biopsy for histological examination. Women who still show evidence of high grade cervical dysplasia will be treated
as per best practise (LEEP, loop excision of the lesion) and followed up appropriately

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Lopimune

Primary outcome measure
Tolerability of Lopimune capsules administered as a pessary in the vagina. After administration of the drug the participants were seen in clinic every 48 hours.They were then asked about any side effects (e.g cervicitis, vulvitis, vaginitis, discharge, vaginal dryness, unusual local sensations such as burning, tingling and numbness and these were recorded on a questionnaire (case report form). This continued for the 2 week duration of the treatment.
Full blood counts and liver function tests were also assessed at 1 week and 2 weeks of treatment with a 2 week post treatment check as an addition.

Secondary outcome measures
Efficacy of Lopimune, as measured by clearance of HPV and resumption of normal cervical cytology/pathology. Participants have a baseline HPV test and cervical cytology screen. In addition they are examined by colposcope using visualisation of the cervix by iodine stain. This is repeated at 4 weeks (i.e 2 weeks post cessation of treatment and 3 months. In addition at the 3 month post treatment time point the participants also have a punch biopsy(s) taken for histology.

Overall study start date
01/04/2013

Completion date
01/04/2014

Eligibility

Key inclusion criteria
1. Women aged above 18 years
2. Patients who freely agree to join the study after extensive information and counselling; must also give written informed consent
3. Patients must be able to receive and understand verbal and written information about the

study
4. Patients ready and willing to comply with the study follow-up schedule
5. Women receiving Lopimune must be HPV positive and have evidence of cervical dysplasia

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Planned 30 - 40 women with high grade cervical disease. (from 600 - 800 screened)

Key exclusion criteria
1. Patients under 18 yrs of age
2. Patients who don't fulfil the above inclusion criteria
3. Patients with conditions in which blood sampling may increase risk of complications eg sickle cell disease
4. Known HIV positive patients
5. Patients whore too ill to give informed consent
6. Persons who it is concluded through clinical judgment by the investigator should not participate in the study e.g. anticipated poor study compliance
7. Patients who have had prior surgical procedures on the cervix eg cone biopsy, hysterectomies etc.
8. Patients with invasive cervical cancer or carcinoma in situ

Date of first enrolment
01/04/2013

Date of final enrolment
01/04/2014

Locations

Countries of recruitment
England

Kenya

United Kingdom

Study participating centre

Research Floor 5
Manchester
United Kingdom
M13 9WL

Sponsor information

Organisation
University of Manchester (UK)

Sponsor details
Oxford Road
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Sponsor type
University/education

ROR
https://ror.org/027m9bs27

Funder(s)

Funder type
Charity

Funder Name
Cancer Research Trust (Kenya)

Funder Name
Caring Cancer Trust (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	29/01/2016		Yes	No