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A trial to establish whether laser treatment of anal precancer prevents development of anal cancer in HIV-positive men who have sex with men

Submission date 15/07/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 15/07/2015	**Overall study status** Completed	
Last Edited 24/05/2019	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Anal cancer is a growing problem in the UK. Almost 90% of these cancers are caused by the human papillomavirus (HPV). HPV infection in a weakened immune system can lead to abnormal cell changes which are graded as anal intraepithelial neoplasia (AIN) 1-3, with AIN 2 and AIN 3 considered to be high-grade neoplasia (AIN 2/3). These changes are called precancers, but it is not known how many, over what time period will turn to cancer. Although many doctors and scientists think we need to treat AIN 2/3 (precancer), as is done in women for cervical precancer to prevent cancer, there is no proven treatment for anal precancer (AIN 2/3) that will prevent anal cancer. Laser treatment may be an effective strategy to prevent anal cancer. The main aim of the study is to assess the long-term effect (up to 5 years) of laser treatment in preventing anal cancer in HIV-positive men who have sex with men with anal precancer.

Who can participate?
HIV-positive men who have sex with men, who have anal precancer

What does the study involve?
Participants are randomly allocated to one of two groups. Participants in the treatment group undergo laser ablation of their perianal (external) or anal canal (internal) disease under local anaesthetic injections. If the disease volume (extent) is large the ablation may be done under general anaesthetic as a day case. Rarely, it may be necessary to treat extensive disease as a staged procedure over more than one treatment visit. Participants in the active surveillance group receive no treatment. All participants are followed up every 6 months with standard examinations. The number of cancers, the effect of treatment on preventing new precancer, quality of life, and the costs of treatment are compared between the groups.

What are the possible benefits and risks of participating?
The main ethical issue is that participants in the surveillance group are not treated, but this is justified for two reasons. First, there is no proven treatment and standard care at present is a

'watch and wait approach' (observation). Second, patients in the surveillance group have the benefit of regular examination, which is not routinely available in the UK. With regular examination every 6 months, anal cancer can be diagnosed at a very early stage, when treatment is less radical and clinical outcomes are excellent (85-90% survival at 5 years). If anal canal lumps are identified at any study visit or through patient self-examination in between visits, the participants are seen at short notice to exclude cancer and referred on to treatment if cancer is found.

Where is the study run from?
1. Homerton Hospital Anal Neoplasia Service (HANS) (UK)
2. Bloomsbury Clinic, Mortimer Market Centre (UK)

When is the study starting and how long is it expected to run for?
October 2014 to September 2021

Who is funding the study?
National Institute of Health Research (NIHR) (UK)

Who is the main contact?
Jennifer Child

Contact information

Type(s)
Public

Contact name
Miss Jennifer Child

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Additional identifiers

EudraCT/CTIS number
2015-002806-36

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
19230

Study information

Scientific Title
A randomised controlled trial to study the effectiveness of Laser ablation versus Observation to Prevent Anal Cancer in men who have sex with men with human immunodeficiency virus infection who have high-grade anal intraepithelial neoplasia (AIN 2 and/or AIN 3) disease

Acronym
LOPAC

Study objectives
The LOPAC study will endeavor to answer the question if active treatment of high-grade AIN disease may prevent progression to anal cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London – London Bridge, 02/07/2015, ref: 15/LO/0942

Study design
Randomised; Interventional and Observational; Design type: Diagnosis, Prevention, Screening, Treatment, Cohort study

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: Cancer; Subtopic: Colorectal Cancer; Disease: Anus

Interventions
The treatment being tested is laser ablation. This involves burning the skin/other similar lining using laser where anal precancer was identified and involves a local burn. Patients in the treatment arm will receive up to four courses of laser treatment during the trial period, performed by one of the clinicians at Homerton University Hospital NHS Foundation Trust. Follow Up Length: 72 month(s); Study Entry : Single Randomisation only

Intervention Type
Procedure/Surgery

Primary outcome measure
Incidence of anal cancer in treatment arm compared to observation arm through the trial period; Timepoint(s): Over course of trial = 72 months

Secondary outcome measures
For all enrolled participants:
1. The rates of AIN 2 and/or AIN 3 detected in the population enrolled into the study.; Timepoint (s): Over the course of trial = 72 months
2. Risk factors for AIN 2 and/or AIN 3 and knowledge about HPV and anal cancer in participants with AIN2 and/or AIN3, compared to those who screened negative for AIN2 and/or AIN3 disease.; Timepoint(s): Over the course of the trial = 72 months
For all randomised participants:
3. Proportion of clearance/regression/progression of high-grade AIN lesions in the treatment arm, compared to the observation arm.; Timepoint(s): Over the course of the trial = 72 months
4. Incidence of metachronous (new) lesions and the rate of recurrence of high-grade AIN disease after clearance in the treatment arm, compared to the observation arm.; Timepoint(s): Over the course of the trial = 72 months
5. Difference, if any, by quadrants of high-grade AIN disease in the treatment arm, compared to the observation arm as measured by the proportion of disease clearance/regression /progression.; Timepoint(s): Over the course of the trial = 72 months
6. Number of treatment episodes/treatment duration needed to clear high-grade AIN lesions, by quadrants of disease in the treatment arm. ; Timepoint(s): Over the course of the trial = 72 months
7. Proportion free of high-risk HPV types in the treatment arm, compared to the observation arm, at the end of the study. ; Timepoint(s): At end of trial = at 72 months
8. Incidence of anal cancer in the treatment arm compared to the observation arm stratified by HPV 16 detection. ; Timepoint(s): Over the course of the trial = 72 months
9. Health-related quality of life, as measured by Area Under the Curve for EQ-5D, in the treatment c compared to the observation arm at each visit post-randomisation. ; Timepoint(s): Over the course of the trial = 72 months
10. Health-related quality of life, as measured by Area Under the Curve for EQ-5D, in the treatment arm only, 1 month post-laser ablation; Timepoint(s): Over the course of the trial = 72 months
11. Total cost of each anal cancer case prevented (including equipment costs and clinic visits). ; Timepoint(s): Over the course of the trial = 72 months
12. A model of AIN grading, progression, regression and clearance as a result of laser ablative treatment. ; Timepoint(s): Over the course of the trial = 72 months
For all trial participants:
13. Anal cancer rates up to 40 years after enrolment in the screened, treated and surveillance patient groups (through a future ethically approved study). ; Timepoint(s): Up to 40 years after enrolment (as part of a future ethically-approved study)

Overall study start date
01/10/2014

Completion date
30/09/2021

Eligibility

Key inclusion criteria
1. HIV-positive men who have sex with men (MSM) over 18 years of age (HIV status confirmed by patient's HIV unit)
2. CD4 cell count of 350cells/µl or greater within twelve months of randomisation; if CD4 count is less than 350cells/µl the patient must be on highly active antiretroviral treatment for at least three months, confirmed by patient's HIV unit
3. Not currently enrolled in any other intervention study about AIN or anal cancer
4. Willing to attend Homerton University Hospital NHS Foundation Trust for all treatment and follow up appointments if allocated to treatment arm of the study
5. Physical and mental capacity to give informed consent
6. Necessary level of verbal and/or reading comprehension of English to give informed consent

Only patients with histologically proven AIN2 and/or AIN 3 disease within the previous four months will be eligible for randomisation for the second part of the trial

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
Planned Sample Size: 3500; UK Sample Size: 3500; Description: We are screening about 3,500 participants. Those without high-grade anal precancer disease will not be asked to attend again. All participants found to have histology-proven high-grade precancer will be invited to continue into the second part of the trial. 660 participants with high-grade AIN disease from the 3,500 enrolled patients will be randomised 1:1 into the treatment and observation arms (N= 330 in each arm).

Key exclusion criteria
1. Previous laser or other ablative treatment for AIN/warts in both the anal and perianal regions (cryotherapy if NOT an exclusion critera; if they previously had ablative treatment for external AIN disease/warts and now present with untreated anal canal disease they will be eligible; and similarly, if they had previous anal canal ablative treatment for AIN disease/warts and now present with untreated external disease, they will be eligible to participate in the trial)
2. Any other topical or surgical treatment for AIN 2 and/or AIN 3 or anal/perianal warts in the previous six months
3. Previous or current diagnosis of anal cancer or under investigation for anal cancer
4. Unable or unwilling to attend treatment and follow-up visits at the Homerton hospital (if randomised to treatment arm) or follow up visits at their recruiting site (if randomised to observation arm)

Date of first enrolment

04/12/2015

Date of final enrolment
02/01/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Homerton Hospital Anal Neoplasia Service (HANS)
Homerton University Hospital NHS Foundation Trust
Clifden Centre
Homerton Row
London
United Kingdom
E9 6SR

Study participating centre
Bloomsbury Clinic, Mortimer Market Centre
London
United Kingdom
WC1E 6JB

Sponsor information

Organisation
Homerton Hospital Anal Neoplasia Service (HANS)

Sponsor details
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christine.inwang@homerton.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.homerton.nhs.uk/

ROR
https://ror.org/00x444s43

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

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

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?

HRA research summary	28/06/2023	No	No