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Assessing the safety, pharmacokinetics and pharmacodynamics of single and 14 days dosing with two vaginal microbicide formulations containing either Darunavir, or Dapivirine and Darunavir.

Submission date
04/02/2015

Registration date
05/02/2015

Last Edited
27/02/2019

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Microbicides are gels, films or suppositories that can kill or neutralize a number of viruses and bacteria. Researchers are currently looking at whether women can use them to prevent becoming infected with HIV through sexual intercourse. A safe, affordable and effective microbicide may help prevent many infections and spread of the disease. At the moment, there are two microbicides which are being tested in large clinical trials for this purpose. Both microbicides use drugs which work against HIV, known as antiretrovirals (ARVs). Both of these microbicides just have one ARV (two different ones) in them. If there was a microbicide with two different ARVs in it, it might work better (be more effective) and it might be less likely to allow the HIV virus to become resistant (a possible danger when using only one ARV). This study will test a microbicide which has two ARVs in it. One of the microbicides in a large clinical trial has the ARV Dapivirine in it. Another very good ARV is Darunavir, which is used widely as a tablet to treat people with HIV, but which has not been tested as a microbicide. A microbicide which has a combination of Darunavir and Dapivirine in it will be compared against a microbicide with only Darunavir in it.

Who can participate?
Healthy women between the age of 18 and 50.

What does the study involve?
The study tests the safety of the two microbicides, and whether the ARVs will neutralise HIV in the vaginal secretions via a pharmacodynamics assay. Participants are randomly allocated into one of two groups. Those in group 1 are given the microbicide containing only Darunavir. Those in group 2 are given the microbicide containing Darunavir and Dapivirine. The effectiveness of the microbicides are first tested after just one treatment and then after the participants have been treated daily over a 2 week period. Genital tract samples are collected from the

participants during these treatment periods. These samples are tested ex-vivo (outside the body) at Janssen in a form of the HIV culture test, which determines whether those secretions can block the replication of HIV in a cell line assay.

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

Where is the study run from?
York Hospital (UK)

When is the study starting and how long is it expected to run for?
October 2014 to June 2015

Who is funding the study?
European Commission - Framework VII (UK)

Who is the main contact?
Mr David Thompson

Contact information

Type(s)
Scientific

Contact name
Mr David Thompson

Contact details
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Additional identifiers

Clinical Trials Information System (CTIS)
2014-003571-27

Protocol serial number
18176

Study information

Scientific Title
A randomised, double blind phase I study to assess the safety, pharmacokinetics and pharmacodynamics of single and 14 days dosing with two vaginal microbicide formulations containing either Darunavir, or Dapivirine and Darunavir.

Acronym

DAPIDAR v2.0

Study objectives
Scientists are trying to develop vaginal products that might be used by women which could stop them getting HIV infection through sexual intercourse. These are called microbicides. The aim of this study is to compare two vaginal microbicide formulations, one containing the single antiretroviral Darunavir, and the other two antiretrovirals (Dapivirine and Darunavir).

Ethics approval required
Old ethics approval format

Ethics approval(s)
14 LO 1762; First MREC approval date 07/11/2014

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Treatment

Study type(s)
Treatment

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

Interventions
1. Blood borne virus screening: Blood sample-taking
2. Cervical biopsy: Tissue sampling
3. Cervico-vaginal examination: Colposcopy and Speculum examinations
4. Diary card issued / collected: Participant to record date/time of IMP administration, and to observations of physical condition between study visits
5. Genital infection screening: Swabs to be taken; Informed consent, To be taken by the study physician prior to starting study procedures
6. Medical history and physical exam: Conducted together, initially to establish eligibility, and then to monitor condition through the study
7. Plasma sample: Blood-sampling;
8. Randomisation: Participant to be assigned to one of the two trial arms, either Darunavir alone, or Dapivirine and Darunavir (randomisation is double-blinded)
9. Routine laboratory parameters: Blood sample-taking
10. Swabs: Vaginal sampling for microbiome and Nugent scoring
11. Urinalysis: Urine sample-taking
12. Urine pregnancy test: Urine sample-taking
13. Vaginal Instead cup sample: Secretion sampling by collection cap
14. Vaginal Weck Cel Samples:Secretion-sampling by absorbent strips

Intervention Type
Drug

Phase

Phase I

Drug/device/biological/vaccine name(s)
1. Dapivirine 2. Darunavir

Primary outcome(s)
Concentrations of IMP in secretions, plasma and tissue; Timepoint(s): 8 and 24 hours after a single dose,
12 and 36 hours after 14 doses

Key secondary outcome(s)
1. Anti-HIV activity in cervico-vaginal secretions using the Tibotec MT4-GFP assay; Timepoint(s): 8 and 24 hours after a single dose, 12 and 36 hours after 14 doses
2. Correlations of Dapivirine and Darunavir levels with anti-HIV activity; Timepoint(s): 8 and 24 hours after a single dose, 12 and 36 hours after 14 doses
3. Number of events attributable to the study gel leading to discontinuation of the gel; Timepoint(s): At any time during the single or multiple dosing periods
4. Number of grade 3 or above clinical or laboratory AEs confirmed; Timepoint(s): At examination or on repeat testing respectively during the dosing or at examination
5. Number of grade 3 or above genital adverse events (AEs); Timepoint(s): During the dosing or follow up period
6. Prevalence of six respective types of vaginal flora; Timepoint(s): pre-dosing, post-single and post-multiple dosing
7. Vaginal slide Nugent scores; Timepoint(s): pre-dosing, post-single and post-multiple dosing

Completion date
30/06/2015

Eligibility

Key inclusion criteria
1. Available for the duration of the study
2. Willing and able to give written informed consent
3. In good health as determined by medical history, physical examination, results of screening tests and the clinical judgment of a medically qualified investigator
4. Judged, in the opinion of a medically qualified investigator, to be able and likely to comply with all study requirements as set out in the protocol
5.Willing to undergo screening for HIV, Hepatitis B, Hepatitis C and sexually transmitted infections (Chlamydia, Gonorrhoea and Trichomonas)
6. Willing to abstain from vaginal practices including sexual intercourse and receptive oral sex from 48 hours before any given dose and up to 72 hours after
7. Willing to abstain from using any genital preparations other than the study gel during the period of gel administration and until the final follow up visit
8. Willing to abstain from using tampons during the two periods of gel administration
9. Willing to refrain from blood donation for the duration of the study
10. If fertile, using a reliable method of contraception for the 3 to 4 menstrual cycles covering the cycles pre study, during study dosing and until the final follow up visit has been completed. For the purposes of this trial only the following will be accepted as a reliable form of contraception:
10.1. Consistent use of condoms with every act of sexual intercourse
10.2. Combined oral contraceptive pill

10.3. Desogestrel containing progesterone only pill (Cerazette)
10.4. Intrauterine contraceptive device or system
10.5. Injectable contraceptive or progesterone implant
11. Willing to undergo a urinary pregnancy test at screening, on the day of randomisation, on the day of receipt of the second dose of the microbicide and at the final follow up visit
12. Have been registered with a General Practitioner (GP) for at least the past 3 months and willing to allow the investigators to discuss the volunteer's medical history with their GP prior to randomisation
13. Agree to registration on a national database of trial subjects to prevent overvolunteering (TOPS), and to the taking of a photograph to be kept at the trial site
14. Upper Age Limit 50 years ; Lower Age Limit 18 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Female

Key exclusion criteria
Untreated syphilis, gonorrhoea, trichomonas, chlamydia, vaginal candidosis or bacterial vaginosis (participants who test positive for any of these infections and are subsequently treated will be eligible provided all other inclusion criteria are met)
1. Seropositive for hepatitis B surface antigen (HBsAg) or Hepatitis C (antibodies to HCV) or HIV
2. Any clinically significant abnormal finding on screening biochemistry or haematology blood tests or urinalysis
3. Abnormal findings on pelvic examination, deemed clinically significant by a medically qualified investigator
4. Irregular menstrual bleeding likely to cause vaginal bleeding during the dosing period as judged by a medically qualified investigator
5. Treatment for CIN or other gynaecological instrumentation of the cervix within the last 3 months
6. An allergy to parabens or any of the other IMP constituents
7. Insertion of an intrauterine contraceptive device or system within the last 6 weeks
8. Any other significant disease, disorder or finding, which, in the opinion of a medically qualified investigator, may either put the volunteer at risk because of participation in the study, or may influence the result of the study, or the volunteer's ability to participate in the study
9. Participation in another research study involving an investigational product in the 3 months preceding enrollment, or planned use during the study period
10. Pregnant, less than 12 weeks postpartum, lactating or willingness/intention to become pregnant during the study
11. Significant concern raised by GP in relation to participation
12. Unable to read and speak English to a fluency level adequate for the full comprehension of

procedures required inparticipation and consent
13. Unlikely to comply with the study protocol

Date of first enrolment
20/10/2014

Date of final enrolment
30/06/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
York Hospital
Wigginton Road
York
United Kingdom
YO31 8HE

Sponsor information

Organisation
York Hospital NHS Trust

ROR
https://ror.org/027e4g787

Funder(s)

Funder type
Government

Funder Name
Seventh Framework Programme

Alternative Name(s)
EC Seventh Framework Programme, European Commission Seventh Framework Programme, EU Seventh Framework Programme, European Union Seventh Framework Programme, FP7

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration