

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

<b>Submission date</b> 04/02/2015	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 05/02/2015	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 27/02/2019	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> 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**  
York Hospital  
Wigginton Road  
York  
United Kingdom  
YO31 8HE

## 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

### **Study design**

Randomised; Interventional; Design type: Treatment

### **Primary study design**

Interventional

### **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 in participation 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