INFORMATION SHEET FOR RESEARCH PARTICIPANT

Study Title: Study on anal human papillomavirus infection and anal intraepithelial neoplasia among men who have sex with men in Indonesia, Malaysia, and Thailand

Short Title: Anal HPV and AIN among MSM in Indonesia, Malaysia and Thailand

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Sponsor: Verein Aids Life through TREAT Asia

You must read and thoroughly understand the information sheet and the consent form for this study before signing your name on the consent form.

Introduction

You are invited to participate in a research study called “Study on anal human papillomavirus infection and anal intraepithelial neoplasia among men who have sex with

men in Indonesia, Malaysia, and Thailand" because you are a man who has sex with men who are seeking for services at the study sites and you may be interested in participating in this study.

Before making decision to take part in this study, please carefully read this document. This document provides the reasons why this study needs to be done and also explains the details about this study. If at any time you have questions or concerns, please feel free to ask the principal investigator's or co-investigator's study team. The study team will answer all the questions and clarify all the concerns to you.

You can ask for advice to participate in this study from your family, friends or your personal doctor. You have ample time to make an independent decision. If you agree to take part, you will be asked to sign the consent form for this study and a copy will be given to you to keep.

Why should we have this study?

Men who have sex with men (MSM) are at increased risk of anal cancer. HIV-positive MSM, even with antiretroviral therapy, have a higher risk of anal cancer and anal precancerous lesions (called high-grade anal intraepithelial neoplasia or HGAIN) than HIV-negative MSM. Anal human papillomavirus (HPV) infection, especially with high-risk types, are the most important risk factors for anal cancer and HGAIN. However, data regarding anal HPV infection and HGAIN among MSM are very limited in the Southeast Asian region.

What are the objectives of this study?

This research project aims to determine the prevalence and incidence of anal HPV infection and HGAIN, and evaluate their risk factors, among MSM with or without HIV infection..Information from this study will support the development of HGAIN screening and treatment guidelines for the countries and the Southeast Asian region.

How many participants will join this study?

An approximately 75 HIV-positive and 75 HIV-negative MSM who attended the study clinics in Kuala Lumpur, Jakarta, and Bangkok will be enrolled. The study will also enroll 185 HIV-positive and 95 HIV-negative MSM who are previous participants of the study entitled "Multidisciplinary services to enhance HIV testing and linkage to care among MSM" (MSM VCT) study in Jakarta, Bali, and Bangkok. There will be approximately 260 HIV-positive and 170 HIV-negative MSM in total in this study

How long will you be in this study?

Newly enrolled MSM will be followed up for 12 months after the enrollment into this study. MSM who are previous participants of the MSM VCT study will only have one study visit at enrollment into this study.

What do you need to do if you decide to join this research project?

After the screening visit, newly enrolled MSM will have three study visits at baseline, month 6, and month 12. MSM who are previous participants of the MSM VCT study will have one study visit.

For "newly enrolled MSM" (Table 1)

Screening visit

At the screening visit, you will be asked to provide an informed consent if you agree to participate in this study. You will receive anti-HIV test along with pre-test and post-test counseling.

Baseline visit

This visit will take approximately 1 hour and you will receive the following procedures.

1. You will receive targeted physical examination and will be asked about basic personal information, cancer history, sexually-transmitted disease (STD) history, HIV risk factors,

smoking and sexual behaviors. If you are HIV-positive, we will ask about your antiretroviral regimen. All participants will also receive risk reduction counseling along with the provision of free condoms and lubricants
2. Anal sample collection: Sample will be gently collected from your anus by trained study physicians or nurses using a moistened swab. Collected sample will be preserved in a liquid-based cytology fluid. In addition, an aliquot of the fluid will be used to test for the presence of HPV.
3. High-resolution anoscopy (HRA): HRA is a procedure that uses magnifying lenses and an intensive light source to examine the anal canal with the application of acetic acid and iodine (Lugol's) solution to aid identification of abnormal anal tissue for biopsy. HRA will be performed by trained physicians
4. Symptom and sign screening for STDs and blood drawn for syphilis testing. Treatment of STDs will be provided along with support for partner notification.
5. If you are HIV-positive, you will also receive CD4 count to determine your immune function and HIV viral load test to measure the level of HIV in your blood.

Month 6 and month 12 visits

This visit will take approximately 1.5 hour and you will receive the following procedures.

1. You will receive targeted physical examination and will be asked about recent sexual behaviors. If you are HIV-positive, we will ask if there has been any change to your antiretroviral regimen. All participants will also receive risk reduction counseling along with the provision of free condoms and lubricants
2. Anal sample collection and HRA.
3. Symptom and sign screening for STD and blood drawn for syphilis testing. Treatment of STD will be provided along with support for partner notification.
4. If you are HIV-negative, you will receive anti-HIV test along with pre-test and post-test counseling.
5. If you are HIV-positive, you will also receive CD4 count and HIV viral load test.

For " previous participants of the MSM VCT study" (Table 2)

Screening visit

At the screening visit, you will be asked to provide an informed consent if you agree to participate in this study.

Baseline visit

This visit will take approximately 1.5 hour and you will receive the following procedures.

1. You will receive targeted physical examination and will be asked about basic personal information, cancer history, sexually-transmitted disease history, HIV risk factors, smoking and sexual behaviors. If you are HIV-positive, we will ask about your antiretroviral regimen. All participants will also receive risk reduction counseling along with the provision of free condoms and lubricants
2. Anal sample collection and HRA.
3. Symptom and sign screening for STD and blood draw for syphilis testing. Treatment of STD will be provided along with support for partner notification.
4. If you are HIV-positive, you will also receive CD4 count and HIV viral load test.

MSM with histologically confirmed HGAIN will subsequently be referred to physicians who have experience in providing infrared coagulation or other treatment modalities for HGAIN management, and would remain enrolled in the study.

Table 1: Schedule of study procedures for newly enrolled MSM participants

Procedures	Screening	Baseline	Month 6	Month 12
Consent	X			
Anti-HIV test (9 ml)/pre- and post- test counseling	X		X	X
Targeted physical examination		X	X	X
Risk reduction counseling and provision of condoms/lubricants		X	X	X
Anal sample collection of cytology and HPV genotyping		X	X	X
High-resolution anoscopy with biopsy		X	X	X
VDRL/TPHA (3 ml)		X	X	X
CD4 count and plasma HIV RNA[1] (9 ml)		X	X	X
Total blood volume (ml)	9	12	21	21

[1] Only for HIV-positive MSM.

Table 2: Schedule of study procedures for previous MSM participants of the MSM VCT study

Procedures	Screening	Baseline
Consent	X	
Anti-HIV test (9 ml)/pre- and post- test counseling[1]		X
Targeted physical examination		X
Risk reduction counseling and provision of condoms/lubricants		X
Anal sample collection of cytology and HPV genotyping		X
High-resolution anoscopy with biopsy		X
VDRL/TPHA (3 ml)		X
CD4 count and plasma HIV RNA[2] (9 ml)		X
Total blood volume (ml)	0	21

[1] Only for previously HIV-negative MSM.
[2] Only for HIV-positive MSM.

Responsibilities of study participants

The study team would like to ask for your cooperation in order to achieve a successful study. We would like to ask that you seriously follow the advice from the study team. Please inform the study team if any adverse events occur to you during participating in this study.

What is the benefit from participating in this study?

You will receive screening for HGAIN in this study. If HGAIN is detected, you will receive appropriate referral to get treatment. In addition, you will receive HIV testing and screening for other STDs at each study visit. If you are HIV-positive, you will receive CD4 count and HIV viral load test at no cost.

Taking part in this research might not necessarily benefit your present health condition or increase the length of your life. However, the knowledge from this study will have an important impact on the development of HGAIN screening and treatment guidelines for the countries and the Southeast Asian region.

What are the possible risks for participating in this study?

Risks associated with phlebotomy: These include pain, bruising, infection, and in rare cases, syncope. To minimize these risks, phlebotomists with training in sterile technique will be employed. In addition, all subjects will be seated or recumbent when phlebotomized.

Answering questionnaires about sexual behavior: You may feel shy or uncomfortable when answering some personal questions such as questions about your sexual behavior.

Loss of confidentially: There is the possibility that your HIV status is accidentally disclosed to others. If you test positive for HIV, you could experience social or economic consequences if that information were to become known by others. The investigators in this study will take precautions to keep all information confidential.

Risks associated with anal sample collection and HRA: The use of swab to collect anal sample may cause uncomfortable feeling but it should not cause pain. The HRA examination may cause minor discomfort. If anal tissue biopsy is needed, anesthetic injection can be somewhat painful. You may have minor bleeding for a few days after a biopsy.

What will happen if you are injured?

If you are injured from taking part in this study, you will immediately receive treatment. The study team will pay for your cost of treating injury from participating in this study. By signing your name in this consent form, you will not lose your legal right.

Extra-visit for adverse events

If you experience any adverse events, please immediately come to the clinic even if it is outside the scheduled visits. The doctor will assess the adverse event and provide appropriate treatment and care to you. You will not need to pay for the cost of treating adverse event that occurs from participating in this study.

Storing of samples

With your permission, your anal samples will be stored. The samples stored will not have your name but rather will be assigned a number. No one in the laboratory will know any personal information about you. With permission from the Institutional Review Boards (IRB), parts of your stored samples may be sent abroad for selected testing, not currently specified, which require extreme expertise.

With your permission, your samples will be stored for no longer than 10 years. The stored samples will be used for future testing to evaluate the inflammatory markers and other STDs. For other tests, permission from the IRB will be required. We will not use your samples for any commercial purposes.

Taking part in the study and leaving the study

Taking part in the study is voluntary. You may decide not to take part in this study. You can withdraw from this study at any time for any reasons without it making any difference to the care you receive now or in the future.

The study doctor may ask you to leave the study before it ends in the following circumstances.

- The study is canceled by the sponsors and regulatory authorities.
- You cannot adhere to the protocol procedure.
- The funding for this study is cancelled or there are inadequate funds.
- There will be harm to you by participating in this study.

Do you have other options?

You may decide not to participate in this study. You can continue to get treatment and service from the study site or choose to receive treatment from other hospitals.

Confidentiality

All information about you will be strictly private (confidential). Only the investigators and medical staff, the sponsor, and the IRBs of Chulalongkorn University, University of Indonesia, Kerti Praja Foundation, and University Malaya Medical Centre, or their

representatives can access the information. If you agree, we will give clinical information to your doctor to help in your medical care.

All study information will be confidential to the extent permitted by applicable law and will not be given to anyone without your written permission except as mentioned above.

For study purposes you must be willing to have results published or shared with other interested parties (other local and federal scientists for example) if you are not personally identified. The investigators will use a code instead of your name on medical records in this study. The code will be known only to study personnel and will be stored in a locked place.

New findings

Any important new information found during the study will be given to you and to your primary care doctor. You will be informed of any new findings that we feel may change your willingness to continue in the study and you will be asked to give consent to participate in the study again.

What are the costs to you?

You will not have to pay for anti-HIV test, HRA with biopsy, anal sample collection for cytology and HPV, syphilis testing, CD4 count and HIV viral load as indicated in the study protocol.

Will you get any payment for transportation and loss of time?

You will be reimbursed for your time. Newly enrolled MSM will have three study visits at baseline, month 6, and month 12. MSM who are previous participants of the MSM VCT study will only have one study visit. Every participant will receive 500 Baht (Bangkok) or Rp 140.00,- (Jakata and Bali) or 51 MYR per visit after the enrollment into this study.

What are your rights as a study participant?

As a study participant, you will have the following rights.

1. You will be informed of the characteristics and the objectives of this study.
2. The medical research procedures including drugs and instruments to be used in this study will be explained to you.
3. The possible risks and discomforts of participating in this study will be explained to you.
4. The possible benefits of participating in this study will be explained to you.
5. Other treatment and care options along with their risks and benefits will be disclosed to you.
6. You will be made aware of the treatment plan if there are any adverse events that occur to you during study participation.
7. You will have the chance to ask questions about the study or study procedures.
8. You will be made aware that by consenting to participate in this study, you can still withdraw from this study at any time for any reason without affecting the care you receive now or in the future.
9. You will receive a copy of the signed and dated consent form.
10. You will have the right to make a decision as to whether or not to participate in the study without influence, threat or deception.

If you feel that you do not get appropriate treatment and care for adverse events which occur from taking part in this study or you are not treated fairly according to what described in the information sheet, please complain to the IRB at your study site.

- The Chulalongkorn University IRB, 3rd floor, Ananthamahidol Building, King Chulalongkorn Memorial Hospital, Rama IV road, Pathumwan, Bangkok, 10330 or at telephone numbers 02-256-4455 Ext. 14, 15 (during official hours)
- Faculty of Medicine University of Indonesia Ethical Committee, Jl Salemba Raya No 4 Jakarta, Phone 2131930373 (during official hours)

- The Kerti Praja Foundation IRB, Jalan Raya Sesetan No. 270, Denpasar, Bali, Phone 361-728916 or 728917 (during official hours)
- Faculty of Medicine University of Malaya Ethical Committee, Kuala Lumpur, 50603, Malaysia Tel: 603 79494422 (during official hours)

Thank you very much for your cooperation.