MISTRAL study, an affiliated EuroSIDA study
Informed Consent Form

MISTRAL study Protocol, v1.0, dated 7JUL21

Protocol title: Gut microbiome correlates of serious AIDS and non-AIDS events

Dear Patient,

We would like to ask you if you would be willing to participate in the **MISTRAL study.**

You decide for yourself whether you want to participate or not. Your participation is completely voluntary.

Please read this participant information carefully or have someone you trust read it aloud to you. Use all the time you need to understand the study. Ask the clinical staff to explain any words or information you do not understand. If you decide to take part in the study, you will always be able to change your mind afterwards. You can withdraw from the study at any time and it will have no consequences to you or your rights.

What is the study about
The MISTRAL study is a new observational study that aims to follow 1000 participants living with HIV across Europe. The study will explore the microorganisms in your gut (called the microbiome) in relation to HIV-1 and investigate changes in the microbiome to support development of new treatment options for people living with HIV.

The MISTRAL study will collect stool and blood samples and gather clinical data as well as information about your diet, time and frequency of defecation, medication history and usage and lifestyle data to investigate the long-term prognosis and outcomes for people living with HIV.

The MISTRAL project stands for:
The Microbiome-based stratification of individuals at risk of HIV-1 acquisition, chronic clinical complications, antimicrobial drug resistance, and unresponsiveness to therapeutic HIV-1 vaccination.

The MISTRAL project is a European Union (EU) Horizon 2020 funded project that aims to explore the impact of the human microbiome on clinical outcomes in people living with HIV.

The MISTRAL study, which is a part of the MISTRAL project, will utilize the long-established network, clinical sites and expertise of the EuroSIDA study, which is a prospective, observational cohort study of people living with HIV that has been collecting observational data since 1994.

Who is eligible for this study
Individuals 50 years of age or older living with HIV-1 and are followed in a EuroSIDA site.

You may <u>not</u>:
- have had myocardial infarction, stroke or any invasive tests for these conditions
- have been diagnosed with AIDS within 5 years of MISTRAL study enrolment
- have non-AIDS cancers (not including non-melanoma skin cancers)
- have had liver failure and renal failure.

What will happen in the study
After your enrolment visit (today), you will receive a stool specimen collection kit to be used at home or in the clinic, which should be returned to the clinic within 48 hours. You will receive instructions on how to collect the stool sample with the stool specimen collection kit. When you return to the clinic within 48 hours, you will submit the stool sample and provide a blood sample of approximately 18 ml. Staff members in your clinic will fill in a MISTRAL Questionnaire with data on your diet, time and frequency of defecation, medication history and usage and lifestyle.

At your next scheduled routine clinical visit between 10-24 months after enrolment, you will provide a second stool and blood sample. Clinical follow-up data will be collected annually for two-four years after enrolment and may be extended based on the availability of project funding.

This study does not test or investigate any treatments and will not interfere with any treatment you may receive at this clinic.

Risk and benefits
Participation in the MISTRAL study presents minimal risk to you. When providing a blood sample, you may experience slight pain, bleeding, bruising, light headedness, anxiousness, and in rare cases, fainting or a blood clot where the needle enters the body. You may also experience slight discomfort when collecting a stool sample. There is no personal benefit from participating, however, the study seeks to improve knowledge about HIV long-term prognosis and the relationship between the gut microbiome and the risk of developing the diseases described above, in order to improve treatment guidelines and advance care and treatment for people living with HIV.

You will not be compensated for your participation in the MISTRAL study.

Who is leading the research
The MISTRAL study is cogoverned by an elected EuroSIDA Scientific Steering Committee of 17 members with broad geographic representation and the MISTRAL Consortium, which consists of 11 academic, private and public sector members.

Sponsor and study coordinator is CHIP, which is an independent research institution at Rigshospitalet in Copenhagen, Denmark.

How is the study financed
The MISTRAL study has received funding from the European Commission Directorate-General for Research and Innovation Horizon 2020 Grant Agreement number 847943 (9,994,383.75€).

What happens to my data
During the study, all information, stool and blood samples collected from you will be de-identified and a unique patient identification study number will be assigned to you. All efforts will be made to keep your information confidential and only staff at this clinic are able to identify you.

The de-identified data from your medical record, information provided in the MISTRAL Questionnaire and stool and blood samples will be sent to the Coordinating Centre (CHIP) at Rigshospitalet in Copenhagen where it is stored, and quality control assessments are performed. After the quality control, the data will be securely sent to be stored in the MISTRAL data repository at IrsiCaixa AIDS Research Institute (IrsiCaixa) in Barcelona, Spain. Your samples will also be transferred to be stored in a sample repository and biobank at IrsiCaixa. Samples will be analysed to fulfil MISTRAL project objectives and stored in the biobank for future research. All data and samples will be stored in accordance with current EU legislation.

Data and samples will be made available upon request to members of the MISTRAL Consortium for analyses. Your clinical data, information provided to your physician on the MISTRAL Questionnaire, and stool and blood collected will be analysed in accordance with the scientific programme in MISTRAL to study the HIV infection and associated diseases. As MISTRAL researchers physically are located at different European universities and hospitals, datasets containing information from your medical record and stool and blood samples will be analysed at other locations than at the MISTRAL study coordinating centre.

Any external research projects will be assessed for scientific relevance by the MISTRAL Consortium and EuroSIDA Scientific Steering Committee and will require relevant ethics approval as well as a signed, EU approved, data transfer agreement.

You will be asked to give permission to allow restricted access to your medical records. They may be inspected by MISTRAL study monitors or a government authority to ensure that the study is being carried out correctly.

What if I change clinic
If you move or transfer your medical care to another clinic participating in the MISTRAL study, the research staff would like to continue to collect information for the study.

With your permission, your physician will contact your new clinic and ask them to continue follow-up in the MISTRAL study at this new institution.

How to withdraw
This study does not in any way interfere with the current or future treatment and care that you are receiving at this clinic. Your participation in this study is completely voluntary, and you can at any time decide to withdraw your participation. Should you choose to withdraw your participation, this will have no consequences for your treatment and care.

Contact person regarding the MISTRAL study at this clinic is:

Name: _____

Department: _____

Phone: _____

SIGNATURE PAGE FOR CONSENT TO PARTICIPATE IN THE MISTRAL STUDY

- I confirm that I have read and understand the information sheet above and have been given the opportunity to ask questions and these have been answered to my satisfaction.
- It has been explained to me that participation is voluntary, and I am free to withdraw from the study at any time and for any reason, without prejudice to my treatment or any other rights.
- I permit that authorised personnel may review my personal information, but identifiable information will under no circumstances be made publicly available.
- I have been given a copy of the Informed Consent Form.
- I permit that my personal data and stool and blood samples collected in the MISTRAL study will be used for the purposes of fulfilling the MISTRAL project objectives. My data will be shared with members of the MISTRAL Consortium and the EuroSIDA Scientific Steering Committee.
- I have been informed of the Appendix containing more information about the processing of my personal data and my rights according to General Data Protection Regulation (GDPR) Article 13.
- I agree to participate in the MISTRAL study.

.....	.....	...../...../.....
NAME OF PARTICIPANT	SIGNATURE OF PARTICIPANT	DATE

Statement from the Researcher:
I declare that the subject has received oral and written information about the study and has had the opportunity to ask me questions. In my opinion, sufficient information has been provided to enable a decision to be taken on participation in the study.

.....	.....	...../...../.....
NAME OF RESEARCHER	SIGNATURE OF RESEARCHER	DATE

Note:
This participant information and informed consent with original signatures MUST be kept in the Investigator Site File. The participant must be given a copy. A copy must be attached to the participant's journal, if applicable.

Participant Information and Consent for Future Biomedical Research

You have already given your consent to participate in the MISTRAL study.

During the MISTRAL study, you will provide stool and blood samples on the day of enrolment (today) and during one of your regularly scheduled annual visits up to two years from today. Today and at your follow-up visit, staff members in your clinic will fill in a MISTRAL Questionnaire with data on your diet, time and frequency of defecation, medication history and usage and lifestyle. Clinical follow-up data will be collected annually for two-four years after enrolment and may be extended based on the availability of project funding. We would like to ask you if we may transfer any of your stool and blood samples to a biobank where your samples will be stored in coded form and used for future research for the understanding of the relationship between the microbiome and clinical outcomes in people living with HIV. The samples will only be used for future research after approval by the research team and governing bodies (EuroSIDA Steering Committee and MISTRAL Consortium).

The analyses can be performed by partners in and outside the EU / EEA (European Economic Area). In all cases, even when sent to a third country (e.g., the USA), this will be done in accordance with the Data Protection Act, Chapter V. Analyses of the samples in the biobank will only be carried out after approval by the relevant authorities. The samples in the biobank will be stored for 25 years, after which the material will be destroyed.

You can withdraw your consent to participate in future biomedical research at any time. However, if you withdraw from the MISTRAL study, this does not mean that your consent to future biomedical research will also be automatically withdrawn. You must specifically request this.

If you want to know more, you are very welcome to contact the attending physician or nurse.

Statement from the Participant:

- I know that participation is voluntary and that I can always withdraw my consent
- I consent to my biological material being stored in a biobank
- I will receive a signed and dated copy of this consent form

.....	.....	...../...../.....
NAME OF PARTICIPANT	SIGNATURE OF PARTICIPANT	DATE

Statement from the Researcher:
I declare that the subject has received oral and written information about the biobank and the information is sufficient for a decision to be taken on the retention of samples. The subject has had the opportunity to ask me questions.

.....	.....	...../...../.....
NAME OF RESEARCHER	SIGNATURE OF RESEARCHER	DATE

Participant Information and Consent for Genomics Research

You have already given your consent to participate in the MISTRAL study.

As part of this study we are collecting blood. In this consent form, we are asking to be able to use part of this blood sample for future genetics analyses.

YOUR PARTICIPATION IS VOLUNTARY
Before you learn about the analyses, it is important that you know the following:

- The decision to take part, or not, is entirely up to you.
- You can refuse to take part in this genomics research and still participate in the MISTRAL study.

WHY IS THIS GENOMICS RESEARCH BEING DONE?
Genes are inherited and control things like hair colour and height. Each person's genes are a little different. The purpose of this consent is to get your approval for future researchers to use your blood specimen for genetic testing (testing on your genes) and other related tests in the future. These tests, when linked with your health information from the MISTRAL study, will help us understand how the genetic makeup of people affects organisms in your gut (called the microbiome) composition and risk of HIV related complications.

WHAT WILL HAPPEN DURING THIS GENOMICS RESEARCH?
There are no additional procedures or blood collections that will happen as a result of your consent. We are only asking to use the sample that is already being collected as part of MISTRAL study for genetic analyses.

HOW WILL YOUR BLOOD BE USED?
Your blood will be used to learn more about the health problems that may be caused by either HIV or changes in your microbiome. This may include tests to better understand why some people have more severe complications (get sicker) than others and why medicines to prevent or treat these infections might work better in some people than in others.

Researchers involved with this blood collection project do not know yet exactly which tests will be done.

You and your study doctor or nurse will not get any results from the tests done on your blood collected for this genomics research. These tests will only be used for research and may not apply to your medical care.

Your blood sample collected for this study will:

- Become the property of RegionH.
- Not be sold or used to make commercial products.
- Not be tested for any specific research study unless the plan for using your blood is approved - based on scientific and ethical considerations - by the EuroSIDA Scientific Steering Committee, MISTRAL Consortium and a special committee (an Institutional Review Board or Ethics Committee) at the researcher's institution.

WHAT ARE THE BENEFITS OF BEING IN THIS GENOMICS RESEARCH?
There are no direct benefits to you for participating in this research. Information learned from the blood collected as part of these analyses may help others in the future.

WHAT ARE THE RISKS OF THESE GENOMICS RESEARCH?
There are few risks involved with your participation in this research. A small but unlikely risk is the possibility of others finding out about your participation in this research.

HOW WILL YOUR PRIVACY AND THE CONFIDENTIALITY OF YOUR INFORMATION BE PROTECTED?
Every reasonable step will be taken to protect your privacy and the confidentiality of your health information and to prevent misuse of this information, and to make sure your blood sample is handled with care at the storage facility. For example, your research records will be identified only by a code. Your blood sample and results of any genetic testing will be identified by a second code. Only a few statisticians (persons who analyze the study results) associated with the MISTRAL study will have access to both codes in order to analyze the test results. These statisticians will not have access to any information that can identify you.

Researchers will write reports, including information they learn from future tests on your blood. These reports will be shared with participating research sites. These findings will also be submitted for publication in scientific or medical journals. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity.

However your records may be seen by:

- Institutional Review Boards (IRBs) or Ethic Committees (ECs) who review the study to make sure it is ethically acceptable
- The National Scientific Ethics Committee in Denmark
- Research staff and study monitors, and their designees.

Staff at [*insert the name of the site*] will handle your personal information very carefully. They are required to make sure that people not involved with this study do not have access to your research and medical records.

Efforts will be made to keep your personal information confidential, but we cannot guarantee complete confidentiality. Your personal information may be released if required by law. Any publication of this study will not use your name or identify you personally.

HOW LONG WILL YOUR BLOOD BE KEPT?
Your blood specimen will be stored for 25 years.

HOW WILL YOUR BLOOD BE STORED?
Your blood specimen will be stored safely and securely at a special facility called a specimen repository located in Spain. This facility follows strict procedures so that only approved researchers can use the stored specimen for future testing. The employees at this facility who will store and track your blood specimen will not have any information that identifies you by name.

WHAT IF YOU ARE INJURED AS PART OF THIS RESEARCH?
If you are injured from having your blood drawn for this research, you will receive proper medical care. The cost for such medical care will be paid by you or another party. There is no program for compensation through this study. You will not be giving up any of your legal rights by signing this consent form.

WHAT ARE THE COSTS TO YOU?
There is no cost to you to participate in this research. The MISTRAL study will cover all costs for storage of your blood and for future tests.

WHAT IF YOU DON'T WANT TO PARTICIPATE IN THE GENOMICS RESEARCH ANY LONGER?

If you sign the consent that your blood can be stored for research to be done at a later date, including studies of your genes, you can change your mind at any time. If you change your mind, specifically let the clinical staff know.

If you decide to withdraw consent for this study, your blood sample, including any parts separated from the sample, will not be used. Every effort will be made to destroy your blood sample and any parts separated from it. If some testing has already been done on your blood sample, the results from this testing will remain as part of this research.

Signature Page for Consent to Participate in the MISTRAL Study Genomics Research (Protocol v1.0, dated 7 July 2021)

I give my consent for the blood sample collected as part of my participation in the MISTRAL study can be used for future genetic research. I understand that the testing and research on my blood sample will be done at a later date. I also understand that my study team and I will not get results from any testing done on my blood sample. Further, I understand that my blood sample may be stored for a long time.

Unless I decide at some point in the future to submit a request in writing to no longer take part in this study, I agree to let the study researchers use my blood sample for approved related genetic testing and research, whether or not I am still alive. I also agree to give permission/authorization for the use and disclosure of personal health information as described in the consent form for the purposes of this research; however my name will not be associated with the information or with the genetic testing results.

I have read this consent form (or had it explained to me) and all of my questions were answered, and I agree to take part in this study.

Name of Participant	Signature of Participant	Date

Name of Researcher	Signature of Researcher	Date