MISTRAL Study

An affiliated EuroSIDA study

MISTRAL Visits and Questionnaire Instruction Manual

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1. OVERVIEW

The purpose of this document is to provide an instruction manual for Principal Investigators (PIs) and clinical site staff participating in the MISTRAL study when completing patient baseline data, patient questionnaire and information on samples collection. The instruction manual should be referenced when completing the MISTRAL Visits in REDCap for all individuals who have consented to participate in the MISTRAL study. Use of the instruction manual increases the likelihood that the questions asked will be consistently understood and answered across all participating PIs and individuals. Standardized language of the definition of terms in the instruction manual will aid in ensuring the data collected will be uniformly interpreted and analyzed for the benefit of people living with HIV.

The MISTRAL Visits Redcap project include:
Visit 1: Patient baseline data form, Questionnaire form and Samples form
Visit 2: Questionnaire and Samples

*Note: The Enrolment form is a separate REDCap form to be completed for new enrolled MISTRAL participants not already in EuroSIDA. Existing EuroSIDA participants should not compete the enrolment form, but they should complete these Visits forms.

2. PATIENT BASELINE DATA FORM

Inclusion and exclusion criteria should be ticked off and date of enrolment entered.

Estimated creatinine clearance <50: Please insert the latest measurement taken. Follow link in the form to calculate creatinine clearance

Child-Pugh C: Follow link in the form to calculate Child-Pugh score

Please also reply yes/no whether the participant has consented to genomics analyses. This is the only way the coordinating centre knows which patients should be excluded from these analyses.

*Please note, there is no tick box whether participants have consented to the biobank for future research, as this is mandatory for participation in the study.

3. QUESTIONNAIRE JUSTIFICATION

The MISTRAL Questionnaire has been developed in order to inform MISTRAL researchers about how participants' diet, time and frequency of defecation, medical history and usage and lifestyle data may or may not impact long-term prognosis and outcomes for people living with HIV.

Before completing the Questionnaire, please restate the purpose of the Questionnaire for the participant.

4. GENDER, BIRTH DATE, STOOL COLLECTION AND DIET INFORMATION

4.1 Patient ID (PID):

The PID code for MISTRAL participants is a 7-digit code, consisting of a 3-digit center code followed by a 4-digit participant code. The participant code for the MISTRAL study starts with 8001 for those not already in EuroSIDA. EuroSIDA participants joining MISTRAL retain their EuroSIDA PID number. You should enroll participants as XXX-8001, XXX-8002, etc. However, please remove the hyphen in the PID code in REDCap and REST. For existing EuroSIDA participants please write their EuroSIDA PID.

4.2 Gender

Please indicate which gender the participant identifies with. Gender identification on the MISTRAL Questionnaire should be the same as stated on the enrolment form.

4.3 Date of birth

Please indicate the participant´s date of birth

4.4 Stool

Date of defecation for current stool sample: date the participant deposited the stool sample

Stool sample received date at clinic: date the participant returned the stool sample to the clinic

Stool consistency as reported by participant based on the Bristol Stool Form Scale for current sample: the participant will provide their stool consistency type on a card with their stool sample to the clinic within 48 hours of collecting their stool sample.

Time of defecation for current stool sample (e.g., 12:30): the time of defecation will be provided by the participant on the stool sample tube label

Average stool consistency (i.e., most frequent type of stool) based on the Bristol Stool Form Scale in the last 14 days: the participant will provide this information orally to clinic staff

Average stool frequency (times per day) within last 14 days: the participant will provide this information orally to clinic staff

4.5 Diet, vitamins, probiotics and alcohol

4.5.1 Current diet classification

The participant will provide diet classification information orally to clinic staff. Initiation of provided diet should be at least two weeks prior to visit.

Please tick the box that best represents the participant's current diet classification:

- ☐ Omnivore: both plant and animal-based diet
- ☐ Pescatarian: plant and fish/seafood-based diet (i.e., a person who adds fish and seafood to a vegetarian diet)
- ☐ Vegetarian: plant-based diet including dairy products and eggs
- ☐ Vegan: solely plant-based diet (i.e., no animal products or by-products)

Please tick the box if the participant has a lactose-free diet AND/OR a gluten-free diet (yes/no):

- ☐ Lactose-free diet: no consumption of products with lactose
- ☐ Gluten-free diet: no consumption of products with gluten

4.5.2 Food Portions:

The participant will provide the following food portion information orally to clinic staff:

- How many days per week does the participant eat red meat?
- Average number of portions of fruit and/or vegetable consumed per day (e.g., one bell pepper, a handful of peas or one apple):
- Average number of portions of dairy/milk consumed per day (e.g., one glass or cup of yogurt or milk (200 ml) or two slices (60 g) of hard cheese or 2 spoons (25 g) of soft cheese):

- Average number of portions of fiber/whole grains consumed per day (e.g., one slice wholegrain bread, ½ cup brown rice, wholegrain pasta or cereal (Please find a list of food fibers in appendix B of this manual)):

4.5.3 Vitamins

The participant will provide the following vitamin intake information orally to clinic staff. (Regularly refers to **daily or 4-6 times a week)** :

- Has the participant taken a multi-vitamin tablet regularly for the last month:
- Has the participant taken a vitamin D tablet regularly for the last month:
- Has the participant taken a vitamin B tablet regularly for the last month:

4.5.4 Probiotics

Participants will specify orally whether they have consumed probiotics, 1) Daily or 4-6 times a week within the last week or 2) Daily or 4-6 times a week within the last month. Participants may also answer 3) none or 4) unknown.

Examples of probiotics include yogurt and yogurt-like products (Kefir, fermented milk, etc.), kombucha, and/or probiotic supplements.

4.5.5 Alcohol

Please indicate the average number of alcoholic beverages the participant drank per week (one alcoholic beverage is equal to e.g., one beer (250 mL), glass of wine (110 mL), or spirit (30 mL)[i].

5. TREATMENT INFORMATION

5.1 Antibiotics

Please indicate whether the participant has taken antibiotics within three months from stool sample collection date (excluding topical treatment (e.g., applied to the skin)).

Please report all antibiotics within three months from stool sample collection date. Indicate start date, stop date and whether the participant is taking the antibiotic at the most recent clinic visit. If treatment is ongoing, please leave stop date blank.

5.2 Antifungal Medication

Please indicate whether the participant has taken antifungal medication within three months from their stool sample collection date (excluding topical treatment (e.g., applied to the skin)).

Please report all antifungal medications taken within three months from stool sample collection date. Indicate start date, stop date and whether the participant is taking the antifungal medication at the most recent clinic visit. If treatment is ongoing, please leave stop date blank.

5.3 Anti-inflammatory Medication

Please indicate whether the participant has taken anti-inflammatory medication (e.g., ibuprofen, etc.) within three months from stool sample collection date (excluding topical treatment (e.g., applied to the skin)).

Please report all anti-inflammatory medication taken within three months from stool sample collection date. Indicate start date, stop date and whether the participant is taking the anti-inflammatory medication at the most recent clinic visit. If treatment is ongoing, please leave stop date blank.

5.4 Hormone Treatment

For women, please indicate whether the participant has taken oral birth control or post-menopausal hormone replacement therapy within one month from stool sample collection date.

For all please indicate whether the participant has taken transgender hormone replacement, oestrogen treatment or testosterone treatment within one month from stool sample collection date

Please indicate the date for latest start and date for latest stop. If treatment is ongoing, please leave stop date blank.

5.5 Proton Pump Inhibitors

Please indicate whether the participant has taken proton pump inhibitors (omeprazole, pantoprazole, esomeprazole, rabeprazole, lansoprazole, or dexlansoprazole) within the last three months

6. SEX LIFE

Please indicate whether the participant receives anal sex or not and whether the participant has received anal sex up to three days before taking their stool sample.

7. DISEASES AND SURGERY

7.1 Gastrointestinal Disease

Please indicate whether the participant has ever been clinically diagnosed with specific gastrointestinal disease (ulcerative colitis, Crohn's, irritable bowel syndrome, chronic constipation, chronic diarrhea, etc.). Please note that anal haemorrhoids or condylomas, or upper gastric diseases are not considered gastrointestinal diseases.

Chronic constipation: infrequent bowel movements or difficult passage of stools that persists for several weeks or longer. Constipation is generally described as having fewer than three bowel movements a week[ii].

Chronic diarrhea: loose, watery stools three or more times a day for more than four weeks[iii]

7.2 Gastrointestinal Tract Surgery

Please indicate whether the participant has had the following:

- Major surgery of the gastrointestinal tract (exception of cholecystectomy and appendectomy) in the past five years:
- Any major bowel resection (surgical removal of part of the colon or rectum) at any time:
- Date of latest bowel resection (surgical removal of part of the colon or rectum):

7.3 Gluten and Lactose Intolerance

Please provide information about the participant's gluten and lactose intolerance:

- Gluten intolerance:
- Diagnosis type of gluten intolerance:
- When was the gluten intolerance diagnosed/reported:
- Lactose intolerance:
- Type of the lactose intolerance diagnosis:
- When was the lactose intolerance diagnosed/reported:

8. LIFESTYLE AND INFANT HISTORY

Please provide information about the participant's lifestyle and infant history:

- Travel outside of current resident country within the last 3 months:
- Pet with fur or feathers living in household within the last month:
- Average exercise per week (in hours) the last month:
  Exercise: Examples of physical activity include aerobic (walking, running, swimming, cycling), muscle-strengthening (strength or resistance training), and flexibility (stretching, yoga, tai chi) [iv].
- Was the participant primarily breastfed as an infant?
- Birth method of the participant, i.e., was the participant delivered via caesarian section or through a vaginal birth.

9. SAMPLES FORM

For visits 1 and 2 stool, plasma and whole blood samples should be registered. When replying "Yes" to plasma and whole blood collection, please enter collection date.

For stool samples, place cursor in the field next to "Scan or type in the barcode for aliquot". Use the barcode scanner to scan the relevant sample vial label into the system or type the code in manually. Repeat for 6 stool samples, 6 plasma samples and 4 whole blood samples.

10. FORM STATUS

Please indicate whether the forms are 1) Complete, 2) Unverified or 3) Incomplete.

Complete: All information has been provided.

Unverified: If there are unresolved queries in the participant information.

Incomplete: Partial participant information has been provided. Site staff will be able to input data on a later date.

11. REFERENCES

[i] https://www.oiv.int/public/medias/7169/oiv-report-alcohol-drinking-guidelines-collective-expertise.pdf
[ii] https://www.mayoclinic.org/diseases-conditions/constipation/symptoms-causes/syc-20354253
[iii] https://www.niddk.nih.gov/health-information/digestive-diseases/diarrhea/definition-facts
[iv] https://ec.europa.eu/jrc/en/health-knowledge-gateway/promotion-prevention/physical-activity