

Protocol Amendment

No. 01

Amendment to MISTRAL Study Protocol. Version 1.0, Dated 7 July 2021

An affiliated EuroSIDA study: Gut microbiome correlates of serious AIDS and non-AIDS events

1. Summary of Amendment

This Protocol Amendment is prepared due to a clarification necessary for MISTRAL protocol.

No update of the original protocol, version no 01, 07 July 2021, has been made.

2. Changes to the protocol

Additions to the original protocol are listed below, with reference to the sections affected.

Text deleted is marked with ~~strike-through~~, while added text is in *italic*.

All assessments will be performed as described in the original protocol.

In cases where changes/additions have been made, the appropriate section has been included in this amendment. Repetition of otherwise unchanged sections have not been included in this amendment.

For the exclusion criteria it is clarified here that the definition of 'AIDS' in the exclusion criteria refers to 'AIDS Infections' (diagnosed within 5 years of MISTRAL enrolment), and hence that experience of all prior AIDS cancers and non-AIDS cancers should be excluded.

Therefore, the following clarification is made:

2.2 Inclusion and Exclusion Criteria

The exclusion criteria are clarified as follows:

- Creatine Clearance <50
- Child-Pugh C end-stage liver disease
- Any ongoing severe life-threatening disease
- Experiencing any of the following events prior to inclusion: myocardial infarction, stroke, an invasive cardiovascular procedure, AIDS-*defining infections* (diagnosed within 5 years of MISTRAL enrolment), ~~and prior AIDS cancer or~~ non-AIDS cancers (~~not including excluding~~ non-melanoma skin cancers)

This clarification does not result in a change in the MISTRAL exclusion criteria.

The clarification described are implemented immediately so study practice reflects that the protocol exclusion criteria has been applied as intended, and the data collection procedures are implemented correspondingly, to avoid sites enrolling participants with previous AIDS cancers or non-AIDS cancers. Since the initiation of the study, it has not been possible to enroll participants with any prior cancers in the REDCap e-CRF, so any previous misconception of the exclusion criteria in the Protocol could not have resulted in the enrolment of non-eligible participants.



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