Protocol Amendment Version 1

Dated 21 July 2023

Study ID: RESPOND Outcomes Study

Protocol for the Outcomes Study, v2.0, dated 29 May 2019

A study in the RESPOND Consortium

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1. Summary

This protocol amendment is prepared to update the current data collection structure in the RESPOND Outcomes Study. The study was initiated in 2017 and the initial protocol required five years of retrospective data collection. As details on the history of a participant since cohort enrolment is central to the study, the data collection wording in section **3.2** and **3.4** has been changed to reflect that. Furthermore, the initial emphasis on integrase strand inhibitor (INSTI) based regimens in the inclusion criteria is no longer necessary, given the widespread us of INSTIs, which is reflected in the updated inclusion criteria in section **5**. These changes have been approved by the RESPOND Scientific Steering Committee and the RESPOND Executive Committee. See more details of this change in the Changes to baseline definition and Inclusion criteria in RESPOND

2. Changes to the protocol

Changes to the original protocol are listed below, with reference to the sections affected.
Added text is in italic.
Removed text in red.

3.2 ENROLMENT

Original

Medical treatment: All HIV medicine, including start- and stop dates and reason for discontinuation. Medical treatment related to co-infections and co-morbidities.

New

Medical *history*: All HIV medicine, including start- and stop dates and reason for discontinuation. Medical treatment related to co-infections and co-morbidities.

3.4 DATA COLLECTION

Original

Study sites/clinics will collect data from participating patients at the time of enrolment, and once a year hereafter. At the time of enrolment, retrospective data are collected up to five years back if relevant and available. Patient record data capture for the Enrolment and FU forms is done by manual data keying or electronically. Manual data keying is performed in a secure online browser-based platform called REDCap. Electronic data capture entails local extraction of data from clinical electronic databases and submission using the RESPOND electronic submission tool (REST) to the RESPOND common data repository. Data is submitted in the HIV Cohorts Data Exchange Protocol (HICDEP) format.

New

Study sites/*cohorts* will collect data from participants at the time of enrolment, and once a year hereafter. Data capture for the Enrolment and FU forms is done by manual data keying or electronically. Manual data keying is performed in a secure online browser-based platform called REDCap. Electronic data capture entails local extraction of data from clinical electronic databases and submission using the RESPOND electronic

submission tool (REST) to the RESPOND common data repository. Data is submitted in the HIV Cohorts Data Exchange Protocol (HICDEP) format. *For both enrolment- and follow-up data submission, all available variables listed in the SOP for data transfer should be submitted from the date of Cohort Enrolment (i.e., do not apply any time limits to supplied data). Cohort Enrolment is defined as the date of first inclusion in the local cohort. A full clinical history must be supplied for participants' ART, AIDS events (including AIDS-defining malignancies) and occurrence of the following non-AIDS events:*

- *Myocardial infarctions*
- *Strokes*
- *Invasive cardiovascular procedures (coronary angioplasties/stenting, coronary by-pass surgery, carotid endarterectomy, and carotid stenting*
- *Non-AIDS defining malignancies*
- *End-stage liver disease*
- *End-stage Renal disease*
- *Fractures*

5. STUDY SUBJECTS

Original

5.1 INCLUSION CRITERIA

1. Signed Informed consent for the Outcomes study, if required by local/national legislation
2. Signed informed consent for the RESPOND consortium and data repository, if required by local/national legislation
3. Age ≥ 18 years of age
4. Confirmed HIV-1 infection
5. Persons receiving integrase inhibitor (INSTI) based antiretroviral therapy if have started after the later of 1/1/2012 and local cohort enrolment (i.e., during prospective follow-up in the cohort and after 1/1/2012) and have a CD4 and HIV viral load in the 12 months prior to starting INSTI or within 3 months after starting INSTI.
6. ART experienced and ART naïve persons not receiving INSTI if have a CD4 and HIV viral load in the 12 months prior to baseline or within 3 months after baseline (here, the latest of 1/1/2012 or cohort enrolment).
7. Persons lost to follow-up or who died before RESPOND enrolment should therefore still be included in the Outcomes study, provided they satisfy the other inclusion criteria.

5.2 EXCLUSION CRITERIA

1. Persons receiving INSTI before 1/1/2012 are excluded from the Outcome study
2. Persons aged < 18 at baseline are excluded from the Outcome study

New

5.1 Enrolment Definitions

*a) **Local_Cohort_Enrolment** is defined as the date of first recorded visit in the local cohort*

*b) **RESPOND_Enrolment** is defined as the latest clinical visit in the local cohort in the RESPOND dataset in which the participant first appears*

*c) **RESPOND_Baseline** is defined as the latest of Local_Cohort_Enrolment or 1 January 2012*

5.2 Inclusion Criteria

1. Signed Informed consent for the RESPOND Outcomes study, as required by local/national legislation
2. Signed informed consent for the RESPOND consortium data repository, as required by local/national legislation
3. HIV-1 positive
4. ≥18 years of age at RESPOND_Baseline
5. Have a CD4 count and HIV viral load measurement available within the 12 months before RESPOND_Baseline or within three months after RESPOND_Baseline
6. Have at least one clinical visit >1 January 2012