***Text in blue is for instruction only and should be deleted.***

***Text in black should be included if appropriate for the trial.***

**Title Data Monitoring and Safety Plan**

**Version *Insert number* 0.0**

**Date issued *Insert date* DDMMMYYYY**

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**Author(s) Name:**

**Signature:**

**Date:**

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**Signature**

**Date**

**Modification history**

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**DATA AND SAFETY MONITORING PLAN**

1. The data and safety monitoring for ***insert trial title*** will use a number of methods:
	1. Central-TR: Central monitoring of trial records.
	2. Central-SDV: Central source data verification.
	3. Automated: Automated data monitoring.
	4. Site visit: Site visit by Monitor.
2. The monitoring aims and activities to be undertaken are outlined in Table 1. We are confident that there will be limited problems with the conduct of the trial as experienced staff have been specifically employed and deployed to run the trial. In addition, on site a second member of staff checks all data entries. We will therefore be undertaking a proportionate approach to monitoring, and in particular monitoring of source data.
3. Submission of data for trial monitoring
	1. To facilitate centralized monitoring, in addition to the timely completion of eCRFs; the site trial team will submit the following documents to the Central Monitor ***insert details e.g. name and/or email address*** using ***insert method e.g. email or postal address:***

|  |  |
| --- | --- |
| **Document** | **Frequency** |
| ***Insert document e.g. pharmacy temperature tracking log*** | ***Insert frequency e.g. weekly*** |
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* 1. When submitting these documents, they should only include the Patient Identification Number (PIN). Other PII (Patient Identifiable Information) including the patient’s name and any patient number issued by ***insert institution*** should be removed or redacted.
1. Central monitoring of trial records (Central-TR):
	1. Will be undertaken by a member of the Study team, e.g. Data Manager, Trial Monitor or in-country Trial Co-ordinator, who will liaise with the Site Trial Coordinator and/or Clinical Lead on Site.
	2. As outlined in Table 1, some Central-TR monitoring activities will be conducted on an ad hoc basis as required (e.g. after IMP shipment), while other activities will be conducted on a routine basis, probably ***insert frequency e.g. weekly*** but this may be altered as required dependent on recruitment rates.
2. Central source data verification (Central-SDV)
	1. Source data available for the trial ***insert CRFs*** completed on the ward rounds and anonymised copies of the laboratory reports.
	2. We will undertake:
		1. ***Insert percentage e.g. 100%*** SDV of ***insert eligibility documents e.g. positive lab test(s) for specify. Insert percentage e.g. 100%*** SDV ***insert documents*** recording the primary outcome
		2. ***Insert percentage e.g. 20%*** of patients will be selected for SDV of all other information. We will monitor the first ***insert number*** of patients assigned to ***insert treatment arm/cohort*** and the first ***insert number***  of patients recruited to the non-treatment arm/cohort and then select patients randomly from blocks (separately for each study cohort), for example 1 randomly selected patient when a further 6 patients have been recruited. To maximize the usefulness of this monitoring, the selection of patients to be fully reviewed might be varied depending on factors such as the deployment of a new study team.
		3. The ***insert percentage e.g. 20%*** may be increased, for whole patients or specific sections, if systematic errors are identified or quality of data completion is lower than expected.
3. Automated data monitoring (Automated)
	1. The ***insert data capture system e.g. MACRO database*** software has been configured to automatically cross-validate across entire patient records according to specific requirements and includes real-time data clarification requests.
	2. For a full list of the automated checks on the database see ***insert document details e.g. Study Definition Details, dated dd/mm/yyyy.***
4. Site visit by Monitor (Site visit)
	1. It is anticipated that the Monitor will conduct ***insert number*** site visit during the course of the trial.
	2. During this visit, the Monitor will undertake the activities outlined in Table 1 central and site monitoring checklist.
5. Reporting monitoring outcomes
	1. With the exception of the site visit, all monitoring activities will be undertaken by the central team in ***insert institution*** and recorded on ***insert document,*** including the aspect monitored and any issues identified. The team at site will be able to view the ***insert document*** and check if there are any outstanding queries this will be located ***specify.***
	2. Any protocol deviations or violations identified, and the actions taken to prevent recurrence, will be recorded on the ***insert document***.
	3. Any issues identified will be reported back to the site as required (by raising as a query on the database) and may lead to changes in monitoring.
	4. Any protocol violations or concerns with data quality identified will be reported to the IDMC.

Table 1 Central and Site Monitoring Check List

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Aim** | **Monitoring activity** | **Method\*** | **Frequency** |
| **1** | **Understanding of and adherence to protocol and trial procedures** |
| 1.1 | All study and SOP training undertaken | 1.1a Review training records: Once during deployment of each Study team, the Monitor will review Training records for completeness, accuracy and compliance with relevant SOPs. | Central-TR  | Once for each team study team member |
| 1.2 | Professional competency of study team | 1.2a Review CVs: Once during deployment of each Study team, the Monitor will review each member’s CVs in relation to their role in the Study Team. | Central-TR | Once for each team study team member |
| **2.** | **Verification of participant existence** |
| 2.1 | All participants exists and attended ***insert institution*** | 2.1a Check ***insert proportion*** of trial participants against names and dates on ***insert clinic lists/document*** | Site visit | Once |
| **3** | **Consent** |
| 3.1 | Informed consent has been gained from the appropriate person for each participant | 3.1a All informed consent forms will be reviewed for compliance with the relevant SOP. This will be done by the Monitor during their site visit and (as this site visit will happen during the course of the trial), the Trial Co-ordinator will review the remaining consent forms at the end of the trial.  | Site visit (and trial co-ordinator) | Once |
| 3.2 | Consent has been recorded  | 3.2a Automated check for Consent is included in the database.  | Automated |  |
| **4.** | **Eligibility** |
| 4.1 | All patients included in the trial meet the eligibility criteria  | 4.1a Each week the Monitor will review patients entered on the database against data recorded on ***insert CRF/document*** | Central-TR | ***Insert frequency e.g. weekly*** |
| 4.1b The Monitor will review compliance against eligibility criteria for all records from source data ***insert percentage e.g. 100%*** SDV on ***insert CRF/document*** and ***specify i.e. lab reports***, where lab reports are available) to check eligibility. | Central-SDV |  |
| 4.1c Automatic check for Eligibility (including EVD positive, age, pregnancy, breast feeding, posing of risk, informed consent) and completeness is included in the database | Automated |  |
| 4.2 | All eligible patients have been invited to take part in the study | 4.2a The Monitor will check once during the site visit, as far as possible, the completeness of the ***insert CRF/document*** against ***insert clinic lists/notes*** (all patients should appear on both lists). This will only be possible if ***insert clinic lists*** are available. When lists are available but it is not possible for this to be done in ***insert percentage 100%*** of cases due to workload, a period of time will be selected ***e.g. two week long*** periods during the course of the study.  | Site visit | Once |
|  |  |  |  |  |
| 4.3 | Ebola positive | 4.3a For all patients where copies of the lab records are available, the Monitor will undertake SDV of the ***insert test and result*** as part of the eligibility criteria.  | Central -SDR |  |
|  |  | **Randomisation** |  |  |
| 4.4 | All patients randomly allocated to TKM and observational cohorts  | 4.4 Each ***insert frequency e.g. week*** all patients randomly allocated to ***insert treatment arm/cohort*** and **insert treatment arm/cohort**, ***insert CRF/document*** will be reviewed for compliance with the randomisation SOP. Information recorded on these documents will also be cross checked against data entered on the database. | Central SDV  | ***Insert frequency e.g. weekly***  |
| **5.**  | **Trial supplies** |
| 5.1 | Integrity of the IMP  | 5.1a The Monitor will review the pharmacy storage Temperature Log ***insert frequency e.g. weekly*** to ensure the IMP was stored within the temperature range specified in the SOP and, in the case of any excursions, the SOP followed. | Central-TR | ***Insert frequency e.g. weekly*** |
| 5.1b The Monitor will review the ***specify documents e.g. shipment Temp Tale, following each shipment, to ensure the IMP arrived within the packaging temperature assured period and within the appropriate temperature range.***  | Central-TR | Once for each shipment. |
| 5.1c The Monitor will review the Pharmacy to ensure the IMP is stored in a locked facility, with limited access and with appropriate set up for temperature monitoring. | Site visit | Once |
| 5.2 | Accountability of IMP | 5.2a The Monitor will review the Drug accountability logs (by vial/bottle)weekly to see that all IMP doses are accounted for. | Central-TR | ***Insert frequency e.g. weekly*** |
| **6** | **Trial data (Outcomes and Adverse events)** |
| 6.1 | Data have face validity | 6.1a Automatic check for data values to ensure are in the expected format and within expected ranges are included in the database. | Automated |  |
| 6.2 | Overall data quality | 6.2a The Central-SDV will undertake a full review of the eCRFs against the source data (***insert CRF/document*** and available ***insert laboratory reports***) for ***insert percentage 20%*** of patient records. Errors within the sample will be identified and any areas of concern raised.  | Central-SDV |  |
| 6.3 | IMP dosing has been conducted in accordance with SOP and accurately recorded | 6.3a The Monitor will review the Drug Accountability log (by patient) for each patient in the ***specify treatment arm/cohort*** (following completion of their course) for compliance with the relevant SOP and check this against the eCRF (checking dosing and outcome) | Central-TR | As required |
| 6.3b The Monitor will check IMP dosing is in compliance with SOP and correctly recorded on eCRF for ***specify*** ***percentage e.g. 20%*** of records included in the Central-SDV monitoring.  | Central - SDV |  |
| 6.4 | Safety reporting is complete and has been conducted in accordance with the SOP.  | 6.4a The Monitor will review all ***specify i.e. SAE/SAR/SUSAR*** forms (in a timely manner) and reconcile the information against the eCRF to ensure accuracy, completeness and compliance with the SOP and regulatory/IRB reporting requirements.  | Central-TR | As ***specify SAE/SAR/SUSAR*** occur |
| 6.5 | Primary outcome data are accurate and complete | 6.5a The Monitor will review on ***insert frequency e.g. weekly*** basis the anonymised ***insert CRF/document*** and check the outcome data recorded on the ***insert CRF/document*** against the eCRF. (***Insert frequency e.g. weekly*** review will be expedited when a ***specify endpoint*** is reached.) | Central-TR | ***Insert frequency e.g. weekly*** |
| 6.5b ***Specify primary outcome data*** will be reviewed to ensure consistency with all data recorded for the patient, as part of the Central-SDV monitoring for ***insert percentage e.g. 100%*** of patients.  | Central-SDV |  |
| 6.5c Automatic checks on ***specify primary outcome data*** are included in the database. | Automated |  |