Data Management Plan

LoW Dose-Intensity vs. Standard Dose-Intensity COntinuous Renal ReplaceMent Therapy in Critically Ill Patients (WISDOM): A Pilot Randomized Trial

Version 2.0

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1. INTRODUCTION

The purpose of this document is to outline the measures taken by the study co-chairs and the coordinating centre for the WISDOM pilot study to ensure that the data collected for the trial is accurate and complete. This document will provide an overview of the three different methods utilized to ensure data quality and completeness with details on the objective of each of these methods and the specific activities performed.

a) Data management reports run on a periodic basis by central coordination team
b) Remote monitoring activities
c) Site Investigator closeout statement

2. DATA MANAGEMENT REPORTS

Study-specific data management reports will be run periodically by the project manager to ensure data quality and completeness. The data quality checks described below are intended to look for:

a) Missing data
b) Inconsistent data
c) Data outliers
d) Protocol deviations

The sections below outline the details of each of the study-specific reports, along with the variables that will be checked, the report description and frequency of each data quality check.

2.1 Eligibility Criteria

Variables: Inclusion Criteria; Exclusion Criteria; Was 'YES" answered for all inclusion criteria?; Was 'NO' answered for all exclusion criteria?

Description: This check is performed to ensure that the eligibility criteria form is completed correctly for all patients randomized into the trial or entered as eligible but not enrolled.

- Response to inclusion criteria is 'Yes'
- Response to exclusion criteria is 'No'

Frequency: Ongoing; manual checks will be performed on an ongoing basis by the project manager

2.2 Informed Consent

Variables: 'Was consent obtained to continue participation post-randomization?'; 'Was regained capacity participant consent obtained?'; 'Please specify why SDM or Regained Capacity consent was not obtained post-randomization'; 'Please specify why regained capacity consent was not obtained'

Description: For patients that are consented using a deferred consent process or SDM consent, this check ensures that:

- Appropriate measures were taken to obtain patient's consent to continue participation in the study post-randomization; and

- If the site was unable to obtain patient's consent post-randomization, an appropriate reason is entered in the database for not obtaining patient's consent.

Frequency: Ongoing; manual checks will be performed on an ongoing basis by the project manager

2.3 Randomization

Variables: 'Was the participant enrolled on the study?'; 'Randomize the participant'; 'Randomization date'; 'Randomization time'

Description: The following checks are performed on the consent and randomization form to ensure that it was completed correctly and that the patient was randomized to the trial:

- 'Was the participant enrolled on the study?' – should be 'Yes'
- 'Randomize the participant' – allocated study arm listed and message 'already randomized' present
- 'Randomization date' – date entered
- 'Randomization time' – time entered

Frequency: Ongoing; manual checks will be performed on an ongoing basis by the project manager

2.4 Timing, Sequence of Events

Variables: 'Hospital Admission Date and Time'; 'ICU Admission Date and Time'; 'Date and Time of Full Eligibility'; 'Date and Time of deferred consent'; ''SDM consent date and time'; 'Participant consent date and time'; 'Randomization Date'; 'Randomization Time';

Description: This report ensures that the study procedures were carried out in the appropriate order.

Hospital Admission > ICU Admission > Eligibility Confirmed > Consent Obtained > Randomization

Note: Eligibility and Consent may occur simultaneously or consent may occur slightly ahead of eligibility as coordinators often work on these simultaneously. In such cases, manual queries will be raised to confirm that the date and time entered is correct.

Frequency: Monthly

2.5 Daily Data

Variables: 'Randomization Date'; 'CRRT Discontinuation Date and Time'; 'ICU Discharge Date'; 'Death in ICU'; # of Intervention – Daily Data Worksheet eCRF instances in REDCap

Description: This report will confirm that there is data entered for every day from Day 0 to CRRT discontinuation, ICU discharge or death. As specified in the protocol, daily data should be collected from date of randomization until CRRT is discontinued or ICU discharge (whichever comes first). Therefore, checks are performed on these variables to ensure that:

- there is data for every day that a participant is alive and receiving CRRT;
- that the CRRT discontinuation date is either on or before the ICU discharge date, or,
- that the CRRT discontinuation date is the date of death

Frequency: Monthly

2.6 Protocol Deviations related to CRRT Initiation

Variables: 'CRRT Initiation Date & Time'; 'Study Allocated CRRT Initiation Date & Time'; 'Day 0 CRRT duration'; 'Day 0 Time in allocated target range'

Description: As specified in the protocol, participants must receive at least a minimum of 12 hours and a maximum of 24 hours of standard dose-intensity CRRT prior to receiving the study allocated dose-intensity. This report checks that the participant receives a minimum of 12 hours and no more than 24 hours of standard dose-intensity CRRT prior to study-allocated dose-intensity.

Frequency: Monthly

2.7 Primary Endpoint - Total delivered effluent flow rate

Variables: 'blood flow rate'; 'dose (total effluent)'; 'dose (hemofiltration)'; 'hemofiltration – pre-filter'; 'hemofiltration – post-filter'; 'dose (dialysate)'; 'dose (total mean)'; 'weight'

Description: This check ensures that all data elements were collected daily in order to analyze for the primary endpoint.

Frequency: Monthly

2.8 Secondary Endpoint - Time in Allocated Dose-Intensity Range

Variables: 'time in allocated target range'

Description: This check ensures that the secondary endpoint for adherence to allocated CRRT dose-intensity can be assessed.

Frequency: Monthly

2.9 Biochemical Endpoints – Electrolytes

Variables: 'serum base excess'; 'serum pH (MAX/MIN)'; 'serum [HCO3] (MAX/MIN)'; 'serum [Na+] (MAX/MIN)'; 'serum [Cl-] (MAX/MIN)'; 'serum [K+] (MAX/MIN)'; 'serum [Mg+] (MAX/MIN)'; 'serum [PO4-] (MAX/MIN)'; 'serum [urea] (MAX/MIN)'

Description: This check ensures that the biochemical endpoints can be assessed.

Frequency: Monthly

2.10 Safety Endpoints - Adverse Events

Variables: 'adverse event onset date'; 'relationship to study treatment'

Description: Check to ensure that:

- The event entered is related to the study intervention
- The event entered occurred while the participant was receiving CRRT.

Frequency: Monthly

2.11 Secondary and Tertiary Endpoints - Day 90 Outcomes

Variables: 'serum creatinine at 90-days'; 'death within 90-days'; 're-hospitalized within 90-days'

Description: Check to ensure that the Outcomes data has been entered.

Frequency: Monthly

2.12 End of Study

Variables: 'Did the participant complete the study and vital status assessment at 90 days?'; 'study end date'

Description: Check to ensure that the information entered for patient's completion of the study is consistent with the information entered on the Outcomes CRF.

- Ensure that study completion date is consistent with 90-day window for patients alive at 90-days.
- Ensure that the study completion date is consistent with date of death.
- For patients who did not complete the full study follow-up to 90-days, check to ensure that the information entered in study completion form is consistent with the data entered in the Outcomes CRF.

Frequency: Monthly

2.13 Outliers

Variables: "baseline serum creatinine"

Description: Check to ensure that the information entered on the patient's baseline serum creatinine is within the expect normal or physiological range.

Frequency: Monthly

3. DATA MANAGEMENT WORKFLOW AND QUERY RESOLUTION

Issues identified through the above-mentioned reports will be queried in REDCap for the site to clarify the discrepancy. Sites will have two weeks to resolve the query. For any queries not resolved within two weeks, a query report will be sent to the site PI and coordinator to confirm they are aware of the queries in REDCap and to request that the queries be addressed. Once query resolution comments are provided by the sites and appropriate changes have been made the project manager will close the query.

4. REMOTE MONITORING PLAN

4.1 Objective of Remote Monitoring Plan

The purpose of this section is to outline the study-specific procedures related to remote monitoring and source data verification (SDV) for the WISDOM trial. This section on remote monitoring outlines:

a) Critical variables
b) Methods utilized to identify potential data quality issues
c) The action taken by central coordination team to reconcile any discrepancies in the data

4.2 Remote Monitoring for WISDOM

This is a multi-centre clinical trial with up to 12 participating sites in Canada. Remote monitoring is performed to ensure that the data collected is comprehensive, accurate and collected according to the protocol and supporting operational documents (Manual of Procedures). The purpose of the SDV is to ensure the following:

a) Patient meets the eligibility criteria for the study;
b) Standard operating procedures are followed for obtaining consent and the process is appropriately documented;
c) Complete and accurate data is entered onto the electronic Case Report Forms (eCRFs)

4.3 Remote Monitoring Activities

Remote monitoring will be performed at all participating sites. This includes targeted SDV of eCRF data on 2 of the first 5 patients randomized at each site, followed by a random 10% of participants enrolled after the initial 5. The critical data variables entered in REDCap will be source verified. A list of these variable can be found in Section 4.3.1. Targeted SDV focuses on the data in the following eCRFs:

a) Eligibility and Enrolment
b) Consent
c) Randomization
d) Baseline
e) Intervention – CRRT
f) Intervention – Daily Data Worksheet
g) Outcomes
h) Adverse Events and Serious Adverse Events
i) Protocol Deviations

The project manager will provide sites with the SDV Tool, which is a document listing key variables for targeted SDV. Sites are asked to complete the SDV Tool and send it to the project manager, along with de-identified source documents for selected variables listed on the SDV Tool. Appropriate instructions are provided to sites on how to complete the SDV tool, de-identify source documents, and send these documents to central coordination team using secure file transfer. If allowed by the site, source documents can also be reviewed by the central coordination team through remote access to a site's EMR. If remote access to the site's EMR is possible and all source documents are available in the EMR, no de-identified documents will need to be provided separately.

Upon receipt of the completed SDV Tool and the appropriate source documents, the central coordination team reviews these documents to ensure that the data is consistent with the data entered on the eCRF. The review includes checking the eCRF entries in REDCap for accuracy and completeness against source documents. The central coordination team maintains a monitoring log of all patients for whom source documents are requested, received, and verified. Variables are marked as 'verified' in the monitoring log, once the review is complete. Urgent issues are communicated on an ongoing basis as needed with the PIs/Sponsor.

A follow up email is sent to the site's Principal Investigator and Primary Study Coordinator once the review is completed. The follow up email includes a summary of the data reviewed, issues identified, and any corrective actions needed. The monitoring follow-up email will include a timeline within which the issues identified must be resolved. If the site is unable to meet this requirement, sites will be asked to contact the project manager immediately. The project manager will work with the sites to resolve issues in a timely

manner.

4.3.1 SDV Variables

All the variables below are included in the SDV tool. Sites monitored are required to complete the SDV tool for all variables that are listed in this appendix. In addition, de-identified source documents will be collected from sites for selected variables as specified in the table below.

Form	Field/Variable	Source Document Required?
Inclusion Exclusion and Enrolment	• All criteria as outlined in the protocol and eCRF • Date and time of eligibility	Yes
Consent	• Date and time of initial consent • Type of consent model • Date and time of Post-randomization consent	No
Randomization	• Date and time of randomization • Allocated Arm	No
Baseline	• Year of birth • Weight • Hospital admission date & time • ICU admission date & time • Baseline serum creatinine	Yes
Intervention - CRRT	• CRRT Initiation Date & Time • Study Allocated CRRT Initiation Date & Time	Yes
Intervention – Daily Data Worksheet	• CRRT Duration • Time in Allocated Target Range • Blood flow rate • Dose (total effluent) • Dose (hemofiltration) • Hemofiltration – prefilter • Hemofiltration – postfilter • Dose (dialysate) • Dose (total mean) • Dose (highest hourly) • Dose (lowest hourly) • Ultrafiltration (total) • Fluid balance (total)	Yes

Outcomes	• CRRT Discontinuation Date & Time • RRT at 90-days • Date of last receipt of RRT • Serum creatinine at 90-days • Death within 90-days • Date and time of death	Yes
Adverse Events and Serious Adverse Events	• Adverse event type • Date of onset • Relationship to study treatment • Expectedness • Stop Date	Yes (for SAEs only)
Protocol Deviations	• Type of deviation • Description of deviation • Date of deviation	No

5. INVESTIGATOR ATTESTATION

Within the REDCap database is an Investigator Signoff form. The purpose of the form is to allow all sites to declare that all possible measures were taken to ensure data accuracy and consistency with data entry guidelines.

The text of the attestation in REDCap is:
'By applying my REDCap electronic signature to this form, I confirm that I am the Principal Investigator (PI) for this study site. I have reviewed all electronic data for this participant and find it to be a true and accurate representation of the participant's records as required by the study protocol.'

The site PIs will be required to attest that the participant data entered in REDCap has been reviewed by a study team member delegated the task of reviewing data entry and electronically sign this attestation for each participant enrolled at their site.