Data Safety Monitoring Board (DSMB) for Clinical Trial

INA-RESPOND
INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

What is a Data Safety Monitoring Board?

DSMB is a group of individuals with pertinent scientific expertise that:

- Reviews, on a regular basis, the accumulated research data from an ongoing clinical trial;
- Advises the sponsor and/or researcher regarding the continuing safety of trial subjects and those yet to be recruited into the research trial
- Advises as to the continuing validity and scientific merit of the trial

Purposes of a DSMB

DSMBs are considered to have "stewardship" of a trial.
The board has responsibilities to both subjects (in terms of safety) and the sponsor (in terms of trial credibility)

❖ Specific purpose of a DSMB includes:
- ➢ Protecting participant safety
- ➢ Ensuring the credibility and integrity of the trial for future subjects
- ➢ Ensuring the timely conclusion of a trial so its results can be disseminated
- ➢ Identify protocol violations that suggest clarification or changes to protocol are needed
- ➢ Identify unexpectedly high dropout rates that threaten the trial's ability to produce credible results
- ➢ Ensure the validity of study results

DSMB Roles & Responsibilities

- Conducting an advisory review of the draft study protocol and study procedures
- Providing suggestions, where feasible for potential solutions to identified problems
- Performing ongoing interim reviews of safety and efficacy data
- May also be requested by the sponsor to conduct emergency reviews of data to assess safety-related issues
- Other : Making recommendation; Maintain meeting record

DSMB Member's Qualifications

- Prior experience.
- Knowledge and understanding of clinical trial.
- Willingness and ability to commit to attending meetings and preparatory review of material.
- Demographic diversity or international representation.
- Should not be affiliated with sponsor, investigators, or study staff.
- Should also not have vested conflicts of interest.
- From multiple disciplines represented:
  - ✓ Trial-specific medical/clinical expertise (e.g., physicians)
  - ✓ Biostatisticians
  - ✓ Ad hoc experts (e.g., bioethicists, scientists, epidemiologists), as needed
  - ✓ Patient representatives, when appropriate

What Kind of Studies Need DSMB?

- Randomized
- Are expected to provide answers concerning a medical intervention's efficacy and safety
- Address critical health outcomes (e.g., life-threatening events)
- May involve high levels of toxicity
- Evaluate an endpoint where the inferiority of one treatment arm has both safety and efficacy implications
- Might require early stoppage for ethical reasons if the primary question has been answered (even if secondary ones have not)

DSMB Activities

- Protocol Review.
- Charter Review.
- Orientation Meeting.
- Regular Meetings : Open Session, Closed Session & Closed. Executive Session.
- Provide reports: interim review report, Verbal Report, Summary Report:, Closed Session Report, Immediate Action Report.
- Making recommendation based on reports.

ReDEFINe (Rifampicin DosE FINding Study): The First Study Monitored by INA-RESPOND DSMB

High-dose Rifampicin for the Treatment of Tuberculous Meningitis: a dose-finding study

Rovina Ruslami, Ahmad Rizal Ganiem, Faculty of Medicine UNPAD / RSUP Hasan Sadikin - Bandung
A Peer Health Granted Study,
Sponsored by Padjadjaran University in Collaboration with the United States Agency for International Development (USAID) and Radboud University,
ClinicalTrial.gov Identifier: NCT no:02169882

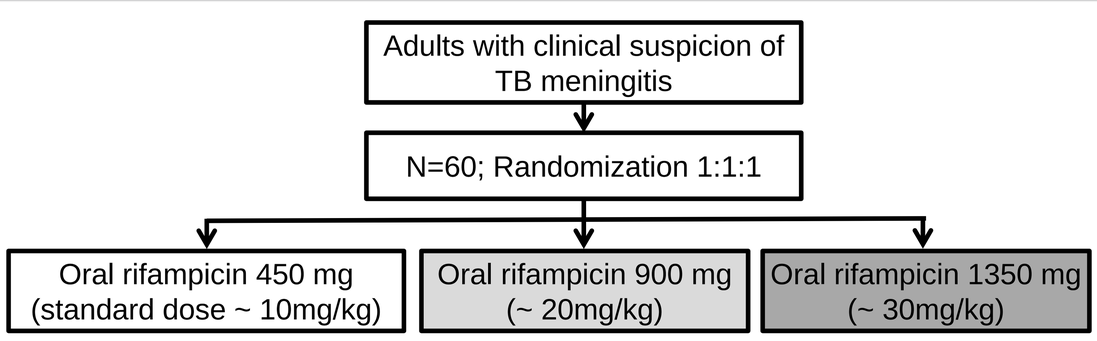
Background & Rationale

- ❖ Meningitis is the most severe manifestation of TB
- ❖ Difficult to diagnose, high mortality.
- ❖ Current treatment regimens: not evidence-based, Follow Pulmonary TB treatment.
- ❖ Rifampicin (RIF) is keystone drug for TBM but its penetration to the Brain Blood Barrier (BBB) is limited
- ❖ Previous study using RIF 600 mg intravenous (iv) found that required RIF concentration in Cerebro Spinal Fluid (CSF) was safer and provided better outcome than the 450 mg p.o
- ❖ However, RIF iv. is invasive, impractical, expensive, and not widely available
- ❖ Alternatively, since the RIF is a friendly and well-tolerated drug, the ReDEFINe study will use higher oral doses

Study Objectives

- ❖ **Primary Objective :**
  To generate PK data of higher dose of RIF in TBM patients.
- ❖ **Secondary Objective:**
  - Safety and tolerability
  - Efficacy, clinical & neurological response
  - Gene-expert for TBM
  - Bio repository of blood, CSF for future research

Schematic Study Design



A Prospective Study , single-center, **double-blinded**, 1:1:1, **randomized**, **placebo** controlled trial Phase IIIb clinical trial (dose-finding study).
Estimation subjects enrolled 60 subjects.

INA-RESPOND Roles In ReDEFINe Study

- ❖ DSMB and Monitoring supported by INA-RESPOND.
- ❖ DSMB Activities scheduled for orientation meeting in November 2014.
- ❖ Purpose of Monitoring:
  - ➢ Protecting human subjects.
  - ➢ Maintaining the integrity of study data.
  - ➢ Compliance with regulations and Good Clinical Practice (GCP).
- ❖ Visit Types of Monitoring:
  - ✓ Study Initiation Visit (SIV).
  - ✓ Routine Site Monitoring Visit (MV).
  - ✓ Study Close Out Visit (COV).

Partners
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