Clinical Trial Data Safety Monitoring Board (DSMB)

Introduction

There are many different issues that may arise during the conduct of a trial that can require drastic decision making by the Data Safety Monitoring Board (DSMB). Trial data and interim analyses often necessitate a reassessment of the scientific validity of the trial, what is clinically meaningful, and what is ethical. This may have consequences such as the modification of:

- the study protocol,
- the trial rationale,
- procedural aspects,
- inclusion and exclusion criteria,
- medication and dose to be used.

When evidence arises that the original assessment of benefit-risk to the participant is no longer favourable, or when the beneficial effect is so evident that it is unethical not to give the treatment to all the participants, then the trial may be prematurely terminated.

All this requires continuous observation of the clinical trial participants and general oversight of the study conduct. In order to ensure this continuous observation, sponsors implement and maintain trial monitoring processes.

Why monitor data for safety?

A lot of data is collected in a clinical trial. It is continuously monitored to ensure that the rights and overall wellbeing of trial participants are safeguarded. It includes

the setup of reporting processes that indicate whether there is a safety matter that requires immediate attention – for example, an unexpected safety signal.

What is a safety signal?

If any concern arises from the data then a safety signal occurs. A safety signal suggests a causal relationship between the intervention and an adverse event or set of related events which is judged to be strong enough to justify further action.

What are Data Safety Monitoring Boards?

A Data Safety Monitoring Board (DSMB) is a group of independent individuals, external to the trial, who are experts in relevant areas. They review the accumulated data from one or more ongoing clinical trials on a regular basis and advise the sponsor about:

- The continued safety of the trial participants.
- The continued validity of the trial.
- The continued scientific merit of the trial.

Does every clinical trial require a Data Safety Monitoring Board?

Although safety monitoring is an essential and integral part of any trial, not all clinical studies require a Data Safety Monitoring Board (DSMB). The creation of a DSMB may be critical for studies that intend:

- To save lives.
- To monitor safety in case of long-term trials even in non-life-threatening diseases.
- To reduce the risk of a major adverse health outcome.

DSMBs are particularly important in studies where interim data analysis is required to ensure the safety of research participants.

Characteristics of Data Safety Monitoring Boards

The main characteristic of a Data Safety Monitoring Board (DSMB) is that it should be free from any political, social, professional, market, or financial influence.

Members of the DSMB are selected and appointed by the sponsor, but they should be fully independent of any ties to the trial, the sponsor, or any other activity or entity that might affect their objectivity.

The size and composition of the DSMB depends on the trial. There are always members with clinical and statistical experience, and members with expertise in ethics and the specific disease area are also often included. The terms and conditions of the appointment of individuals to the DSMB should be transparent, and the procedures of the DSMB should be clearly defined and well documented.

Are patients included on Data Safety Monitoring Boards?

The inclusion of expert patients or other representatives of patient organisations in Data Safety Monitoring Boards (DSMBs) is a relatively recent development. When they are included, patient representatives are equal participants of the DSMB, and their work is bound by strict confidentiality. Patient representatives in DSMBs help to protect the patients and participants’ best interests with valuable inputs such as the patient experience of living with the given disease.

How do Data Safety Monitoring Boards work?

The establishment and management of the Data Safety Monitoring Board (DSMB) is prescribed by a document (charter) developed by the sponsor. The DSMB convenes when pre-determined analysis points are met – for instance, when 50% of the participants of the trial have reached six months of treatment.

At this time, the sponsor submits a report to the DSMB to consider in light of specific questions. Usually, the DSMB only receives the sub-set of data that is relevant to the questions they are considering. This data is cleaned and analysed, often still blinded. The DSMB may request further data for analysis or for the blind to be broken according to rules that are laid out in the charter. The charter must clearly state which members of the DSMB are allowed to have access to any unblinded data.

The DSMB then carefully and rigorously analyses the data and arrives at a recommendation, preferably after reaching a consensus. This process must be carefully documented in order to ensure transparency and ethical appropriateness. The recommendations made by the DSMB must be clearly supported and the justifications for them documented.