DMC Webinar Recap Q & A

Q: For blinded, phase 3 studies, there is an unblinded and blinded medical monitor from a CRO utilized. During the DMC open session, are attendees limited to just Sponsor (Safety, Clinical Development, Project Management) and independent biostatistician. Should CRO medical monitors be invited to attend open session?

A: The sponsor can choose whomever they would like to attend the open session, but it is usually restricted to those people that will be presenting to the DMC or might be needed to answer any questions. The attendees are usually representatives from the sponsor, the ISRG, and the DMC.

Q: Can you speak a bit about the programming changes you referred to?

A: As additional data is collected in the study the TLFs often need to be modified to account for the new data. This could mean the addition of visits to a table or a figure or adding new presentations per the request of the DMC.

Q: Medical Monitor vs DMC? Can you highlight scope/lens and limitations?

A: The medical monitor is usually reviewing safety events on an individual level whereas the DMC is reviewing safety data aggregated by treatment group.

Q: Have you experienced if the DMC recommend to pause recruitment to get more long term data on the enrolled patients before making a decision?

A: Yes, I have experienced a situation where there is an enrollment pause but it was done by the sponsor and the DMC was informed. I am sure there are cases where the DMC has requested the pause in enrollment to accumulate more safety data before exposing more subjects to the intervention.

Q: Can you explain the expected differences in roles between the Sponsor and DMC Biostatistician? Is the DMC biostatistician usually a voting member of the DMC, and are there concerns if they are employees of the CRO managing the DMC?

A: The sponsor statistician is usually blinded to treatment group and should not be looking at aggregate data by treatment group until the end of the study. The DMC statistician is tasked with looking at the aggregate data as the study is ongoing and is a voting member of the DMC. At WCG we do ISRG and have one of our statisticians as the DMC statistician as this could cause a conflict of interest.

Q: Will we receive the slides at the end of the presentation for our reference?

A: Yes

Q: Are the DMC minutes (open or closed) to be shared with the sponsor during the study?

A: The open minutes are always shared with the sponsor shortly after the meeting. The closed minutes will not be shared with the sponsor until after the trial is completed and the sponsor is unblinded.

Q: The IRB will want to see some documentation from the DSMB as to what was reviewed and their recommendation as to whether to continue, halt, or close the study.

A: This is something that needs to be discussed between the sponsor and the IRB.

Q: Is there a point with trying to keep the DMC unblinded at long as possible, eg by initially showing masked treatment group data (eg naming them Group A and B, instead of Active and Placebo)?

A: WCG always uses semi-blinded treatment groups, and it is up to the DMC members to ask for the unblinding codes. Some members want to stay blinded for as long as possible and other want to know the groups right away.

Q: What's the impact if study should have included DMC but did not. Will results of the study be unacceptable?

A: The results may end up being acceptable but there may be issues of study conduct that were left unmonitored and therefore the interpretation of the data may be difficult.

Q: Does the DMC share responsibility in reporting adverse events/findings to the FDA?

A: Typically, the DMC does not report anything to the FDA or any regulatory agency.

Q: Is it too late to add DMC in an ongoing study?

A: It has been done but it can be messy, and it is not optimal. Sometimes a DMC must be added after a study starts because the FDA insists on it.

Q: Can you discuss audits of the DMC and auditors confirming the charter and applicable activities are being adhered - blinded and unblinded (i.e. reconciliation and maintenance of minutes, data packets, etc.)?

A: Generally, the DMC would not be audited but the sponsor may audit the ISRG to make sure that they are following all their SOPs in regard to the support of the DMC. The auditors would only be able to review minutes/reports from the open session while the trial is ongoing, they would not be able to see closed reports/minutes or the recommendations.

Q: If committee members are not told the name of a drug to keep others from seeing, when are they told?

A: The unblinding of the treatment group labels would occur during the closed session of the DMC meeting.

Q: In this day and age of easy data access, does it make sense to have real time data access for DMC members - granted this will be blinded data for the most part?

A: The DMC reviews most data aggregated by treatment group so having access to real time data would not necessarily be helpful. There are some tools like Spotfire and R Shiny that allow the DMC to visualize the data in a different way during the meeting, but the data still needs to be extracted and analysis datasets created before this can happen so they are not viewing real-time data.

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A: Already answered above.

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