Editorial

Impact of COVID-19 Pandemic on Clinical Research and Actions to Overcome - A Summary

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Coronavirus pandemic has led to multiple challenges concerning the management and conduct of ongoing clinical trials, which include restrictions at health care facilities, changes in the availability of staff, unidentified possible interactions, and many more. There might have been a situation where the trial participants, or any/some of the site staff or even for some instances an Investigator might have to self-isolate or be infected by SARS-CoV-2.**(**1**)** Availability of an Investigational Product (IP) was another major issue during the situation and hence the health of the participant. All these factors might have an impact on the accrual, assessment, and provision of clinical trials **(**1**).**

Initiation of a new clinical trial was not possible during this pandemic not only because of the staff availability issues but the regulatory bodies had stopped approvals for non-COVID-19 new trial registration unless requiring an expedited approval in the event of public health emergencies and even some of the submitted trials had approval but were asked not to initiate the recruitment. **(**2**)** A different level of feasibility was expected for the new trials and for enrolling new participants during these testing times considering an update to the risk-benefit section of the protocols which now was expected to have the risk assessment done and the mitigation plan for the identified risks one of which could be, "that the participant and trial workers could encounter due to COVID-19." **(**3, 4**).**

One of the principles of ICH-GCP speaks about the importance and necessity of Ethics Committee (EC) approval for any and every clinical trial protocol before the trial begins, what in case of the new clinical trial for the current outbreak? How do we seek approval in an expedited manner,

where the proposal to the EC will have very limited information, and with the available piece of information EC will have to plan and expedited meetings which would be a virtual one or an unplanned/unscheduled full committee meeting **(**5**)**? E.g. French EC had approved a clinical trial for hydroxychloroquine within 1 day of submission **(**6**)**.

In an Indian situation, there is a big difference between standard care for critical illness available in private and public hospitals. As trials conducted in severe COVID-19 will require robust intensive care support, they are likely to be conducted in private hospitals. This would deprive socioeconomically disadvantaged who visit public hospitals from getting benefits of participation in the trial. It would be desirable to conduct a centrally supervised trial by a government agency to allow all COVID-19 patients to be considered for enrolment in clinical trials irrespective of their socioeconomic status. **(**7**)**

The EC is responsible for closely monitoring the conduct of the clinical trial. However, this would be difficult as the study conduct processes – consent, recruitment, follow-ups, clinical procedures, and serious AEs – would be managed by the investigator and her team rapidly while attending to the critically ill patient. Furthermore, the EC members cannot physically meet the patient or the site in a potentially infectious environment. A review of scanned documents could be an option. Otherwise, the monitoring should be conducted when the study is completed to ensure that the investigator team complied with the protocol and good clinical practice during the conduct of the trial. **(**7**)**

Regulatory bodies, such as CDSCO (Central Drugs Standard Control Organization), EMA (European Medicines Agency), and FDA (Food and Drug Administration) have laid down guidelines for the management of clinical trials during the current pandemic without compromising the participant's safety, rights and well-being. (8, 9, 10) These mainly focused on the risk-benefit considerations by the authorities where the priority is given to the safety of the subjects and impact on the health.

For any trial affected by the pandemic, study reports are expected to include notes of all contingency measures which were put in place towards the maintenance of the trial integrity, in additional the report should also include a list of participants affected by changes related to COVID-19 disruptions and analyses addressing how the changes may impact the trial, especially trial's safety, and efficacy results. **(**11**)**

Regulatory authorities state that the rights, safety, and well-being of trial participants are and will continue to be of paramount importance during the COVID-19 pandemic. **(**9**)** Changes to trial conduct should be acceptable and feasible from the operations and participant's point of view and should be communicated clearly to active/recruiting sites. To support its implementation, changes and local implications must be made clear, including marking of changed documents with track changes. Agreements may be documented as an e-mail exchange. **(**12**)** In continuation, even the participants should be informed about the changes or deviations well in time, these changes may include cancellation of visits, change in laboratory testing, delivery of IMP, etc.

EMA also mentions the additional compensation guidelines for such exceptional times, it says "to implement urgent measures for the protection of participants involved in a clinical trial, expenses may arise which may be borne initially by the participants, these should typically be compensated subsequently by the sponsor via the investigator. If additional financial compensation is provided to sites/investigators (e.g., to cover the cost of using couriers for IMP delivery), this needs to be documented and performed according to national legislation. Handling of reimbursement of such expenses should follow national legislation and/or guidance." **(**9**)** Considering the lockdown and its rules, in such situations to avoid the participant from traveling to the site for the routine visits and exposing them to additional risk, they will be expected to have a video visit, telemedicine would come into the picture and the IMP is expected to be delivered to patients residence which can be managed by the sponsor's team or the site to take care of such situations.

Understanding the current scenario across the globe, every clinical research professional or associated individual is expected to continue the ongoing clinical trial keeping subject's rights and safety on top priority, sponsors are expected to have clear communications with the sites and also allow certain deviations which would not harm participants health. Ethics committees are expected to be available for expedited meetings or connect for the reviews virtually where face-to-face meetings are not possible.

Clinical Trials cannot stop, they need to be planned, managed, executed, and reported knowing the huddles and issues. -by Dr. Kaushal Kapadia

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