ITCC Trials and the COVID19 Pandemic

The COVID-19 pandemic has wide impact on many clinical activities, including the conduct of clinical trials. Throughout this difficult time, it is important that the safety and well-being trial participants are protected, while also ensuring the on-going integrity of the trial data. All trials needs to remain compliant with the trial protocol as well as with EU and national rules. It is acknowledged that national provisions and approaches differ.

The FDA and EMA have provided guidance to trial sponsors on adjustments to the management of clinical trials and participants during the COVID-19 pandemic. The link to the EMA information can be found at

https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19#advice-on-clinical-trials-section

During the COVID19 pandemic, it is understood that individual institutions will apply different guidance on the clinical research activity. This may impact on a range of study activities, including site activation and recruitment of study participants. The status of the COVID-19 pandemic is rapidly changing and guidance may continue to evolve over time, however, it is important at all times that to ensure the safety of patients already recruited on trials.

If any changes are advised at your centre that could impact on ITCC trial participants, it is important that you notify the relevant trial Sponsor, Industry or Academic. It is crucial to maintain good communication with the Sponsor during these challenging times.

Summary of the main principles outlined in the EMA recommendations:

The guidance understands that pragmatic actions may be needed during these challenging times to ensure the rights, safety and wellbeing of trial participants as well as considering the impact in terms of time and staff resources at sites during the COVID-19 pandemic.

On-going trials:

General principles: The trial's sponsor will communicate with investigators any changes they are putting in place for their trials. They will also notify you of actions you could consider at your site that are permissible for their trial. **It is important that all sponsors and investigators follow the specific national legislation and guidance that has been put in place, for example the specific circumstances for submission of substantial and non-substantial amendments**.

The types of measures that could be implemented are:

- Conversion of physical visits into phone or video visits
- Postponement or complete cancellation of visits to ensure that only strictly necessary visits are performed at sites
- A temporary halt of the trial at some or all trial sites;
- Suspension or slowing down of recruitment of new trial participants
- Extension of the duration of the trial
- Postponement of activation of new sites
- Arrangements for treatment or investigation at other sites

Protocol Deviations: It is accepted by the EMA and National Regulatory Bodies that more protocol deviations related to the COVID 19 situation are likely during this period, nevertheless **all deviations must be fully documented at sites and managed by the Sponsors in accordance with their standard procedures.**

The EMA have advised that a proportionate approach to such deviations will be taken but reporting and documentation will be essential and the events and their implications to the trial need to be recorded in the end of study report.

Changes to monitoring and audit: the conduct of trial monitoring and audit activities need to be re-assessed by the sponsors during this period and adjusted to provide proportionate oversight during this period that continues to ensure patient safety and trial integrity but minimises the risk of COVID 19 infection and reduces the workload. Local and national restrictions need to be considered for trial staff at site with regard to on-site monitoring. Temporary alternative arrangements could include postponement of on-site monitoring visits and adaptations to the monitoring plans to allow increased centralised monitoring and remote source data verification, if this is feasible and compliant with national legislation, including privacy laws.

Changes to IMP distribution: there may be some circumstances where the supply chain of an IMP may need to be altered to reduce the frequency of attendance of patients to the trial site.

The types of changes that could be foreseen include provision of a larger amount of IMP to the trial participant than normally prescribed, taking into account the stability of the IMP or trial sites could arrange delivery of the IMP directly to trial participants to avoid the trial participant attending the site. In both circumstances, arrangements for **on-going supervision of the continued treatment by the investigator for example by phone or video-clinic visits are essential**.

There may be circumstances where the sponsor may need to arrange direct supply of IMP to trial participants or that patients need to be transferred to an alternative trial site if there are local reasons for the treatment not being delivered at the normal site, for example local IMP shortage or local staffing issues. National permissions on direct sponsor to trial participant IMP supply vary and it is essential that Sponsors consult with the relevant National Competent Authority regarding these types of amendments to trial conduct.

Initiation of new trials during the COVID 19 pandemic

In most countries, the initiation of new trials during the pandemic is restricted to trials aimed at testing treatments or diagnostics for COVID 19. For the paediatric oncology community, it is frustrating not to be able to progress new trials during this period, however the ITCC and SIOPE community are continuing to work on the development of new trials, so that when this period of restriction is over, we will be in a position to launch new initiatives as rapidly and efficiently as possible to enable our patients have access to innovation and new treatment options.