The spread of the coronavirus and the exceptional measures taken to prevent it also affect the conduct of clinical trials and necessitate the introduction of certain changes. At the same time, it should be sought to ensure the continuity of clinical trials, especially in patients where continuity of treatment is of paramount importance, e.g. oncology patients.

General considerations

Restrictions already and expected to be applied (quarantine, visitation ban in healthcare institutions, increased burden of the healthcare system, possible supply problems for medicines — IMP and non-IMP, etc.) a thorough risk assessment of ongoing investigations should be carried out and measures should be put in place to prioritise patient safety and data validation. In the event of conflict between these two objectives, patient safety should be prioritised.

Please note that all decisions must be followed by the ich gcp and european and Hungarian legislation, including the GDPR.

It should be stressed that patient safety is our top priority and that, consequently, any changes should be proportionate and subject to a thorough risk assessment (benefit-risk assessment, impact on the health and safety of the impacts). The risk assessment shall be repeated and properly documented, depending on the evolution of the situation, even several times.

Any deviation from current practice should be proportionate, verifiable and clearly documented (see ICH GCP 5.0.4).

If you have difficulty obtaining original signatures (wet ink signatures), alternative documentation tools (e.g. printed e-mail) may be acceptable.

In Hungary, the electronic package leaflet and the consent form are not permitted as required by the current legislation, which is also to be followed in an emergency.

During the transition period, the number of protocol deviates may increase. It is important that these derogations are clearly documented (see ICH GCP 4.5.3). The authorities will take a fair approach when reviewing derogations if they are in the interests of participants and do not expose them to undue risk.

For risk groups (immunosuppressant treatment, over 60 years of age, chronic diseases) particularly at risk of coronal virus, special consideration should be given to continuing the study.

In general, it is considered prudent to stop the enrolment of patients during this period.

Licensing practice

If a temporary relocation of a testing site takes place, notification shall be sufficient to continue the investigation at a new site.

When substantial modifications to the study are required in order to ensure the patient's continued participation, sponsor may do so as an "urgent safety measure" (USM). The change will take effect immediately. The urgent safety measure should be sent to the authority and the amendment should be subsequently, officially, authorised in accordance with the usual procedure.

Inspection visits

Sponsor, in agreement with the investigator-in-charge, shall consider converting or deferring on-site visits to telephone visits or terminating them on the basis of the risk assessment, in order to ensure that it is strictly necessary visits to the test sites.

If the epidemiological situation subsequently so requires, consideration should be given to the transfer of subjects to existing or new test sites. Such relocation may only be carried out with the agreement of the subjects and the study leaders (transfer and host), by appropriately transforming the eCRF to ensure that the new test site has access to all information and previously collected data, and to record new data. The relocation agreement should be documented in the TMF (e.g. by e-mail).

If it is not possible to continue the study at a test site, it shall be suspended and everything is followed to ensure patient safety and data adequacy.

Monitoring

In order to reduce on-site monitoring, appropriate alternative methods should be preferred. Alternative methods shall be decided on the basis of a risk analysis taking into account patient and data security in agreement with the test sites and amended the Monitoring Plan on the basis of accepted changes.

The choice of alternative methods shall take into account that they do not place a disproportionate burden on the test site and staff.

Remote and central is monitoring through the EDC system may be an appropriate alternative, focusing on data that is most important for the safety of subjects and the quality of the data.

Monitoring the following indications without checking the source data:

medical history, ePRO and e-journal data, results of physical examinations and protocol compliance with concomitant medicines;

protocol deviating in the EDC (visit outside the window, time of IMP treatment, dose and dose titration, SAE report, application of withdrawal criteria, etc.);

patient safety observations, e.g. deviations in lab results, adverse events and other assessments or lack thereof.

The sharing of patient data and the remote access of the Sponsor's representative to the electronic database of healthcare institutions are not acceptable due to the protection of particularly sensitive data and ethical considerations.

It is important to stress that proper follow-up of these transitional measures after the normalisation of the situation is essential and includes, for example, an increase in the frequency and/or time of on-the-spot monitoring in order to identify and address the possible adverse effects of the transitional measures.

IMP care

Measures to address problems with access to investigational medicinal products and other medicinal products used in the clinical trial (non-IMP) shall be taken in accordance with the procedure laid down in Article 13 of The GMP. It shall be established in accordance with the procedure referred to in Article 10(2) of The Processes may be carried out by a qualified and delegated person on the basis of written regulations.

The transfer of test preparations between test sites, the care of patients on the spot for longer than originally planned, or the dispatch of imp from the test site to the patient's home may arise.

Any transitional measure shall be designed in such a way as to ensure that

the prescribed conditions for transport/storage of the product in question during transport and storage in the patient's home, especially in special circumstances (e.g. 2-8 oC),

safe custody of preparations,

and the relevant documentation of the accounts.

It is recommended to maintain an adequate kit to prevent imp/non-IMP deficiency if it is difficult to deliver them to the test site.

Our Institute undertakes to evaluate clinical trials for the treatment/prevention of Covid-19 by an accelerated procedure.

Our institute strives to provide all necessary support to those involved in clinical trials. We are constantly updating our information, please continue to monitor it.

Budapest, 2020. 16 March