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Indications regarding the management of interventional clinical trials with drugs during the current COVID-19 emergency in Italy

Carmine Pinto ,[1,2] Celeste Cagnazzo[3,4]

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[1]Medical Oncology Unit, AUSL-IRCCS of Reggio Emilia, Reggio Emilia, Italy
[2]President of the Federation of Italian Cooperative Oncology Groups (FICOG), -, -, -
[3]Research and Clinical Development Unit, Pediatric Oncology and Hematology Unit, University of Turin, Turin, Italy
[4]President of the Italian Data Manager Group (GIDM), -, -, -

Correspondence to
Dr Carmine Pinto;
pinto.carmine@ausl.re.it

INTRODUCTION

The Federation of Italian Cooperative Oncology Groups (FICOG), promoted by the Italian Association of Medical Oncology, brings together the 17 Italian oncological cooperative groups that have developed cancer research in Italy (APRIC, ASTRO, GIM, GIOGer, Foundation GONO, GISCAD Foundation, GOIM, GOIRC, IGG, IMI, ISG, ITMO, MANGO, MEET-URO, Michelangelo Foundation, NIBIT Foundation and MITO). The FICOG, in collaboration with the Italian Data Manager Group, in accordance with the Italian Medicines Agency Communications,[1 2] European Medicines Agency Guidance[3 4] and the Recommendations of the Italian Ministry of Health[5], herein provides some indications on the management of interventional clinical studies with drugs in the course of the current emergency for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic, in order to make the behaviour of the clinical trial centres homogeneous, appropriate and safe.

GENERAL PRINCIPLES

The guarantee of the safety of each patient is the general principle to follow, also prevailing with regard to the benefit expected from the study, and consequently a careful and adequate risk assessment is required before any action foreseen by the protocol for patients enrolled is taken. The justifications for any deviations from the protocol are possible if deemed necessary to ensure the patient's well-being and safety through documentation in the records and timely communication to the sponsor. The pre-eminent role of the investigators in charge of the satellite centres with respect to that of the promoter must be considered, with regard to the risk assessment and any deviations from the protocol (to be communicated in a timely manner to the promoter of the study).

PRACTICE INDICATIONS

The opportunity (also considering the operational situation of the staff of the trial centres) must be evaluated before taking the decision to: (A) start a new clinical study, (B) activate new centres and (C) enrol new patients. An assessment of the entire activity and potential outcomes (taking into account avoiding the compromising of the safety of enrolled patients already undergoing treatment and data validity) must be performed before taking the decision to close a centre or the entire trial study. The possibility of temporary suspension of the protocol can be considered in the event of closure due to blocking of activities or new allocation of a trial centre for patients with COVID-19. The investigator responsible for the centre concerned must carefully evaluate whether the trial staff is able to guarantee the continuity of the experimentation. The transfer of patients undergoing active treatment to the nearest trial centre can be envisaged, without prejudice to: (A) the exchange of information between the investigators of the centres involved and (B) the sharing of clinical information and study material. The sponsor must notify the ethical committees of reference of a substantial amendment for immediate implementation.

The follow-up visits of patients at the trial centre should be reduced to those strictly necessary (eg, by converting examinations into telephone contacts or postponement of examinations). For patients with ongoing therapy (chemotherapy, immunotherapy, target therapies and radiotherapy), it is recommended to guarantee the safety of oncological treatments by providing dedicated filters, routes and areas and recommending to the

patients and medical and nursing staff that they comply with the main rules for containing the contagion. In the event that the patient cannot go to the centre (eg, for a patient outside the region; excessive danger of contagion at the centre), it is possible to organise an oral drug shipment from the hospital pharmacy to the patient's home; the entire route (courier, modality) must be managed by the sponsor, except for the availability of personnel at the centre who organise the shipment. Any deviation in the protocol procedures must be documented and adopted in agreement between the sponsor, the hospital pharmacy and the investigator responsible for the centre concerned.

The tests and procedures (laboratory, imaging and instrumental) performed in structures close to the patient's home (for which it is necessary to notify the sponsor) can be considered as valid for the study. The supply of experimental drugs to the pharmacies in the centres could present problems in consideration of possible forced and unexpected closures of the providers in charge. It is advisable to check the quantities of experimental drugs present at the pharmacia of the trial centres, possibly agreeing with the pharmacy on a resupply able to guarantee the presence of a sufficient stock to cover the expected use possibly over the next 2 months.

The sponsors of the clinical trials must modify their monitoring plan. The visits to the centre can be transformed into remote monitoring, avoiding an excessive load of activities on the staff of the trial centre. In the case of update calls (especially for centres with printed records), you can proceed without further authorisation, while in the case of video calls, monitoring with access to electronic records (even restricted) or sending anonymous documentation, the sponsor must request prior authorisation from the Institutional Data Protection Officer. The sponsors will have to reimburse any tests and procedures already paid by the patient (eg, for patients from outside the region) and all the extra costs incurred by the centre (eg, courier delivery for sending the drug to the patient's home).

PHARMACOVIGILANCE

The possible reductions of personnel in the trial centres and the possible manifestation of adverse events, even serious ones, in patients included in the studies require a high level of attention in order to guarantee their identification and timely reporting. Telephone and email contacts with the trial centres can be considered useful for the detection of safety

PATIENTS WITH SARS-COV-2 POSITIVITY

The enrolment in studies of new patients with known positivity to SARS-CoV-2 is strongly discouraged. As regards to patients already undergoing trail treatment and for whom an SARS-CoV-2 infection is documented, these will have to be carefully evaluated especially in consideration of the general clinical characteristics and the ongoing trial treatment and therefore consider a delay and/or a suspension of treatment, also based on the ratio of risks (for the individual patient and for the community gaining access to the centre) to expected benefits of the treatment itself

ETHICS COMMITTEE

The Ethics Committee is authorised to meet in web conferences. It is possible to activate urgent procedures according to decisions and procedures provided for by the individual ethics committee. The emergency procedures may be provided to allow the ethics committee to evaluate them and therefore the timely activation of studies relating to SARS-CoV-2 infection.

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ORCID iD

Carmine Pinto http://orcid.org/0000-0002-3159-5268

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