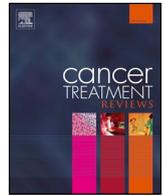




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Hot Topic

Oncology clinical trials during the COVID-19 outbreak: Lessons learnt during the crisis and future opportunities



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ABSTRACT

The COVID-19 pandemic affected many activities in the healthcare system including oncology drug development. Clinical trial recruitment was temporary halted in many centres to reduce patients and healthcare workers' potential exposure to the virus. Conversely, to continue offering treatments for patients already on effective therapies, multiple actions were timely put in place, resulting in simplification of trial-related procedures for patients and clinicians' best interest, reduction of the operational burden and effective communication. Here, we suggest maintaining effective measures for future trial simplification and to expedite drug development.

Starting in the city of Wuhan in China in December 2019, the coronavirus COVID-19 spread through Asia, Europe and US reaching a pandemic scale that paralyzed the entire globe. Thousands of deaths were registered in only a few months. Many activities in- and outside hospitals significantly slowed down, oncology drug development included [1,2].

In our centres in the UK, as in many other countries, recruitment of patients into oncology trials was put on hold [3]. This was certainly a controversial decision to take in unprecedented times, but the main reason for this was to protect patients, their families and clinical staff from the potential exposure to the virus while receiving treatments with not yet fully established benefits. Conversely, patients already enrolled onto trials before the outbreak and receiving treatments for their cancers were offered continued access to experimental drugs. In order to protect patients and clinical staff multiple effective and pragmatic actions supported by regulators, sponsors and clinical teams were put into place within weeks.

These included minimising the number of protocol required procedures including blood tests and hospital visits. Importantly, clinical teams were empowered to perform telemedicine consultations, allowed to ship oral investigational medication (IMP), and to modify treatment schedules for intravenous drugs where indicated. Similarly, to protect administrative staff and monitors, remote monitoring and virtual meetings were quickly and safely established.

The current ongoing oncology trials will teach us whether this pragmatic approach had any negative effects on patient safety and trial outcome. However, in our opinion, clinical teams, regulators and pharma/biotech sponsors adapted quickly to continue to support our patients within the Good Clinical Practice (GCP) framework and we expect any impact to be negligible. Importantly, a positive effect in limiting the amount of bureaucracy and unnecessary procedures for patients, investigators and clinical trial teams has already been observed.

In this context, we want to take the opportunity to invite sponsors, Contract Research Organisations (CROs) and clinical teams to reflect on the 'status quo' on how we perform oncology trials and how we can restart trials with a fresh and more pragmatic approach once this crisis is over.

To be precise, in recent years, the delegation of many activities like trial set-up and monitoring through CROs not only added another layer of complexity between investigators and sponsors, but also added a number of extra-requirements which significantly increased the level of operational burden [4]. Although patients' safety remains the utmost priority, the GCP principles did not change significantly since the Declaration of Helsinki in 1964, but in contrast, an exponential increase affecting trial set-up efforts, trial execution procedures, data recording, monitoring and auditing has been observed [5,6].

Hence, we feel taking this unprecedented situation as an opportunity to accelerate clinical trial simplification for the benefit of our patients, clinical teams, CROs and sponsors. Here we propose the following:

- The number of patient visits should be relevant to the mechanism of action of the drug and kept to a minimum. We understand the value of close medical monitoring in first-in-humans trials when unexpected toxicities may occur during the dose-finding phase of a new IMP; however, we feel that there is a number of visits that could be left to medical discretion based on patients' conditions and comorbidities, especially for late stage trials. Research Ethics Committees (REC) should specifically look at the number of avoidable procedures to ensure patient safety, but also to avoid unnecessary hospital visits. Telemedicine consultations, digital monitoring through devices and local blood tests should be allowed when deemed safe. Quality of life and patient reported outcome measures frequently analysed in trials can be performed via electronic devices by the patient at home. Simplification may significantly spare investigators and administration time, increase the performance of each clinical trial unit and the quality of the care delivered.
- Data and monitoring: too many times investigators are asked to document non-significant events just as a matter of acknowledgment which creates an excess of documentation, requests of amendments in patients' notes and time spent in futile exercises with irrelevant clinical impact. We appreciate the importance of data entry in a timely fashion to warrant safety monitoring and identification of

drug-related toxicities. During COVID-19 outbreak, remote monitoring was successfully implemented, and significantly reduced times for monitors and local staff including costs of travel (not to mention the positive environmental impact). Importantly, clinical staff noticed a significant reduction in requests for unnecessary and non-trial relevant documentation.

- Communication: many patients receiving treatment during COVID-19 required an urgent adjustment of trial procedures which were frequently communicated directly by investigators and agreed by medical monitors. This facilitated approach between sponsor and investigator worked well and should always be available in the patients' best interest. Administrative channels, essential for data recording and trial logistic, should be clearly separated for effective and appropriate communication levels.
- Trial set-up: centres are commonly selected by sponsors based on the investigator experience and historical quality on execution of trials. The number of internal and external approvals required to implement a new trial should be minimised to guarantee a timely trial activation – with the current ongoing COVID-19 trials we witness a pragmatic approach to achieve that; for example the NIHR processed 21 trials within weeks including regulatory and institutional R&D approval [7].

The COVID-19 pandemic significantly affected everyone's life, reminding us of our fragile nature, our limited time and our main priorities, challenging what is superfluous and futile. We do not want to forgive this lesson. Let's together take this opportunity to focus on what is essential, effective and meaningful, for the benefit of our patients, healthcare providers and oncology drug development.

Declaration of Competing Interest

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Employment – Hospital Corporation of America.

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Employment – Hospital Corporation of America.

Honoraria – BeiGene; Bicycle Therapeutics; Guardant Health; Merck KGaA; Roche; SERVIER.

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