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Cancer Research Ethics and COVID-19

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The COVID-19 pandemic is affecting every aspect of medical care delivery, with projections indicating an escalating and indefinite impact upon our daily lives[1]. Clinical oncology research participants are a particularly vulnerable population at this time, due to both their underlying condition and increasing uncertainty about the conduct of clinical trials during a global pandemic.

Robust protections for clinical trial participants are well established in the form of clinical trial design and oversight, supported by caring and dedicated clinical and research staff. However, several considerations become increasingly important in the current situation, and researchers and clinicians treating patients enrolled in research must weigh these carefully.

While we fully recognize the dynamic nature of the COVID-19 pandemic and its constant evolution in degree and scope[2], as the medical ethics editorial team for *The Oncologist*, we would like to take this opportunity to discuss three clinical research ethics considerations that are critical for our cancer research community.

1: Non-abandonment

Non-abandonment is typically a consideration for clinical care rather than clinical research. However, patients on experimental oncology protocols with palliative or curative intent have a strong interest in remaining on trial. Thus, while clinical trial researchers are not classically recognized as having fiduciary duties with regard to research participants, the complex intersection of care, therapies, and experimental interventions inherent to clinical oncology research requires a more nuanced understanding of the overlap between research and clinical obligations.

Despite the profound disruption of a global pandemic to daily clinical duties, tens of thousands of patients with cancer will continue to depend upon their providers to care for them, address their concerns, and direct therapeutics appropriately. For multiple reasons, aspects of this care will be altered in form and schedule. But every effort will be necessary to maintain and continue cancer-directed experimental therapies for patients with imminently life-limiting malignancies, whether they are surgical, radiation-based, and/or drug-based. Creative delivery systems such as tele-health, home infusions, remote laboratories, utilization of satellite facilities, and others will be critical.

In addition, we need to be mindful that patients with cancer may well be some of those at the highest risk of poorer outcomes if they are infected with COVID-19. In China, overall case fatality for those

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without comorbidities was 0.9%, but was 6% for those with cancer[3]. WHO data are similar: the unadjusted fatality rate for those with no co-morbidities was 1.4% but 7.6% for those with cancer[4]. In a small study of 2007 hospitalized patients in China, cancer patients' fatalities were significantly higher (39% vs 8%.)[5]

We must balance this information with the need to provide patients with the cancer-directed interventions upon which they depend. If projected workforce shortages due to infections and familial obligations strain the clinical research staff as anticipated, it is likely that role evolution will occur, with cancer providers and researchers distributed across other roles within the delivery team.

The central message should be that COVID-19 will impact the way clinical and research teams interact with research participants, but that our overarching commitment to be available, in contact, and providing experimental and therapeutic interventions in the best way possible should persist. Available and trusted resources for COVID-19 related caretaking should be disseminated broadly[6].

2: Flattening the curve

One of the clear messages from the CDC indicates that the most effective way to slow the COVID-19 pandemic and ultimately save lives is to "flatten the curve" of new infections[7], spreading them across a larger time-continuum such that limited resources (e.g. hospital beds, ventilators, and clinicians) are less strained at any given time point. As we all know, oncology trials are resource-intensive, and approved protocols frequently require significant in-person contact between participants and research and clinical staff. That said, it is critical that we follow CDC recommendations for screening patients and isolating any with fevers/symptoms, postponing non-essential in-person visits, cancelling those solely for data collection/research, and arranging for telemedicine interactions as much as possible. These steps are directed towards the dual goals of protecting both our clinical workforce and our often-immunocompromised participant population. Since availability of providers to care for patients is crucial, all efforts must be made to increase supply of personal protective equipment so that exposed providers will be protected and continue to care for their patients.

Protocol deviation is an important consideration for both research ethics and compliance, and the National Institutes of Health has recently released several helpful notices regarding federally-funded human subject research trials during the COVID-19 pandemic. These include encouraging investigators, together with their IRBs, to consider "limiting study visits to those needed for participant safety or coincident with clinical care" as well as conducting visits virtually[8]. FDA has issued similar guidance[9]. Every effort to document the nature, timing, and reason for any protocol deviations will be critical to ensure that regulatory and funding oversight can be updated once we are out of the current crisis.

We must also be prepared to honor research participants' right to stop their participation in any clinical trial, for any reason, including if they judge that the extra visits and procedures are too risky in this environment.

3: Emotional support

The psychosocial impact of this pandemic remains unclear but will undoubtedly be profound[10]. Patients with cancer are already psychologically strained and are generally insufficiently screened and treated for related mental health concerns. In addition, those involved in clinical research have unique issues and perspectives related to their dual roles as patients and subjects[11]. Psycho-oncology caretakers and resources will be particularly critical during this time period and, where possible, may be provided remotely through online or phone support.

Lastly, we would be bereft to ignore the psychosocial impact of the pandemic on our research teams, who may be isolated from their typical emotional support resources. Enabling close (virtual or phone) contact with the research team to air concerns, share best practices, and allow for continued community building is also vital[12].

Conclusion

The COVID-19 pandemic is progressing with relentless speed and will further test the clinical and research infrastructure for all of us[13]. Patients with cancer enrolled in clinical trials remain intensely vulnerable to their underlying condition, infection with COVID-19, and to the stressors impacting health care delivery in general. Clinicians and researchers alike are behooved to consider how best to protect participants' health and interests, and to support their collective well-being even during our most challenging moments. We know that we, as a cancer research community, are up to the task.

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