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The Impact of the COVID-19 Pandemic on Oncology Clinical Trials

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Abstract

The COVID-19 pandemic has created unprecedented disruptions to clinical trial research across the world due to a temporary global suspension of patients' recruitment to cancer clinical trials. Here within we present the negative impact of the COVID-19 pandemic on cancer clinical trial activity at the Clinical Trials Ireland Unit at the Mid-Western Cancer Centre. In the first six months of 2020 directly compared with the same period in 2019 there was a 33% (147 V's 99) reduction in patients screened for participation and a 60% (37 V's 15) reduction in patients consented to clinical trials within our unit. At the same time, the COVID-19 pandemic has led to increased clinical research activities in regard to the development of treatments, diagnostics and vaccines to control the pandemic. Extrapolating our observations from the swift implementation of COVID-19-related clinical trials, we discuss strategies to improve the design and conduct of cancer clinical trials.

Background

In December 2019, the novel coronavirus SARS-CoV-2 emerged from the city of Wuhan, resulting in the clinical syndrome of coronavirus disease 2019 (COVID-19) [1]. To date, over 46.2 million cases and almost 1.2 million COVID-19 related deaths have been reported worldwide. The first verified case of COVID-19 in the Republic of Ireland was documented on 28th February 2020. Since then, over 62,000 confirmed cases and greater than 1,900 COVID-19 related deaths have occurred [2]. The COVID-19 pandemic has disrupted all aspects of clinical care delivery worldwide.

Patients with cancer are a vulnerable population, at high risk for contracting COVID-19 and experiencing adverse events [3, 4]. Early studies from Italy, a country greatly affected in the early weeks of the global pandemic, revealed that 20% of COVID-19 related deaths were amongst patients with underlying cancer, most of whom were receiving systemic anti-cancer treatments (SACT) [5].

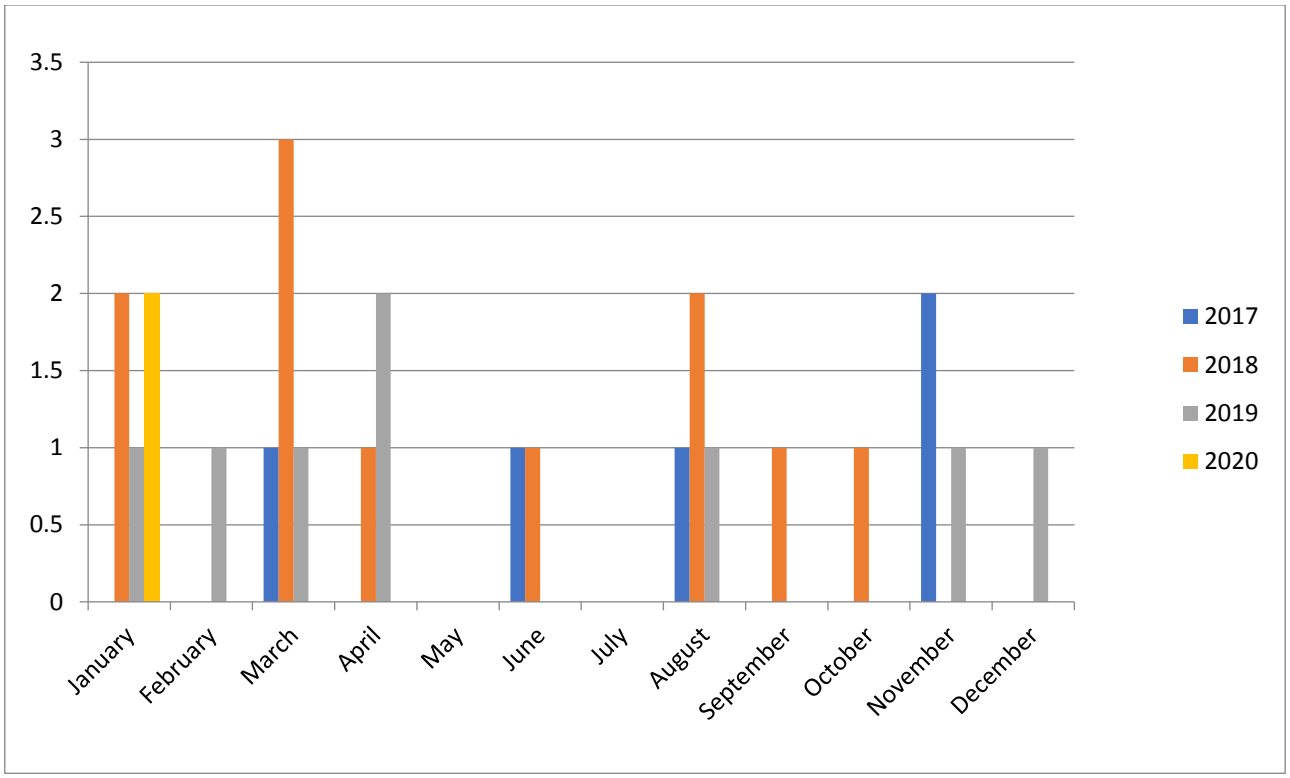
On March 12th, the Irish Government initiated a national lockdown of non-essential services. This nationwide, severe disruption resulted in several changes to the way in which the medical oncology services were delivered across the country's eight cancer centres and their satellite units. Cancer care providers focused on limiting cancer patients' exposure to people infected with the virus and asymptomatic carriers, while attempting to continue routine SACT and access to cancer clinical trials. The European Society of Medical Oncology (ESMO) and the American Society of Clinical Oncology (ASCO) issued guidance on managing oncology patients during the pandemic [6, 7]. In the UK and Ireland, the National Health Service (NHS) and the National Cancer Control Programme (NCCP) have subsequently developed local guidance [8]. This has resulted in changes to the delivery of care, including transfer of inpatient care to private hospital facilities and transfer of the ambulatory delivery of SACT to off hospital sites where possible, as well as introducing virtual solutions for outpatient appointments [4, 8].

In addition, the COVID-19 pandemic has resulted in a worldwide disruption to clinical research. Oncology clinical trials are essential for advancing cancer treatment [9, 10]. Over the last 25 years, thousands of patients in the Republic of Ireland have been enrolled in and benefited from over 400 cancer clinical trials nationwide. In addition, these clinical trials have enabled patients to access novel and potentially beneficial treatments that would not be available for them outside of the trial. It is well documented that patients enrolled into clinical trials have a better outcome due to better treatment options and best clinical practice procedures [11].

Impact of COVID-19 on Mid-Western Cancer Clinical Trials Unit

The Cancer Trials Ireland has an extensive network of over 15 research units throughout the country, all of which have been impacted by COVID-19 pandemic. We aim to illustrate the impact of the COVID-19 pandemic locally on the Clinical Trial Unit at the Mid-Western Cancer Centre, University Hospital Limerick (UHL). Learning from this negative impact, in collaboration with our global colleagues in clinical research, we seek to identify opportunities for transformation of our structures to ensure our vitality and longevity, providing continued meaningful clinical trial opportunities.

The Cancer Clinical Trials Unit (CCTU) at the Mid-Western Cancer Centre opened in 2002. It has established itself as a leading centre for innovative and translation oncology clinical trials in the country. Over the last 4 years 25 clinical trials have opened here, across a variety of primary disease sites, with 5 trials opening in 2017, 11 in 2018, 7 in 2019 but only 2 in 2020 to date (Figure 1).There are a further four expected to open before the end of the year.



New Trials Open: 2017 – 2020 (Figure 1)

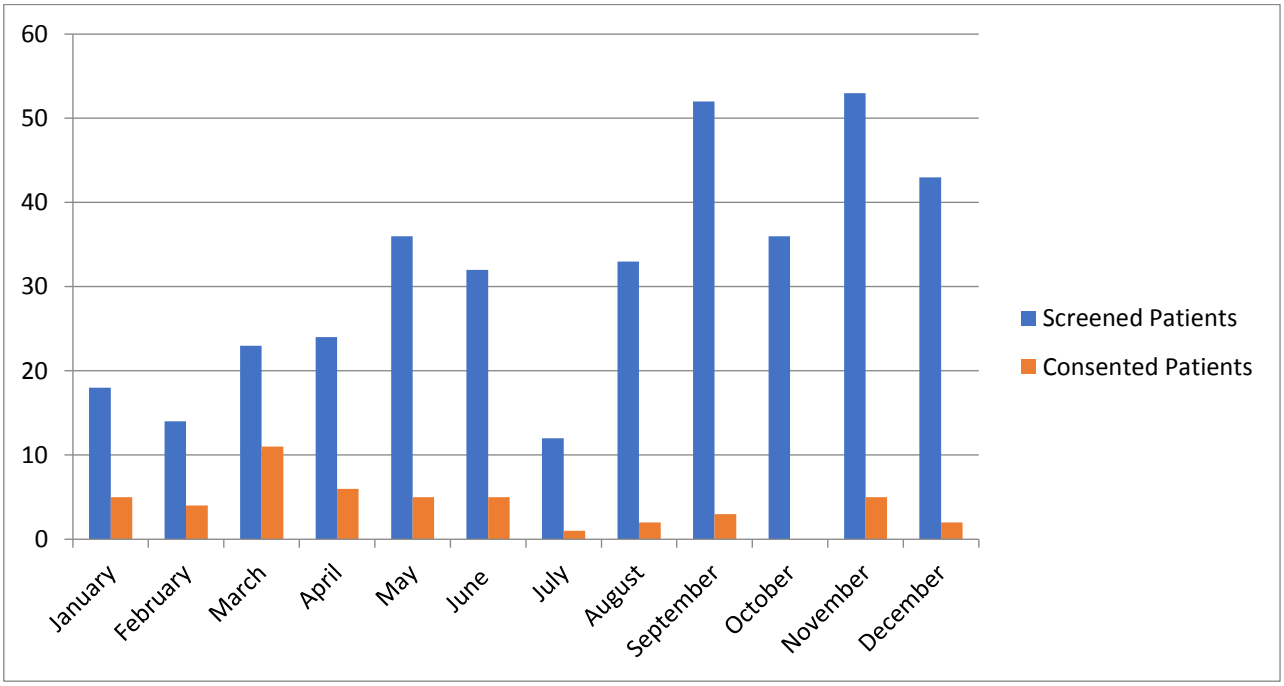
The disruption of the activity of the CCTU due to global COVID-19 pandemic has the potential to impact the scientific integrity and patient safety of ongoing clinical trials, increasing operational burdens on clinical trial programs, and as a consequence, limit access to trials and newer therapies for cancer patients [9, 10, 12]. In response to this, regulatory authorities like European Medicine Agency (EMA) and The Food and Drug Agency (FDA) have produced guidance on all aspects of the ongoing conduct of current trials [13].

This year as the global COVID-19 pandemic affected Ireland, only few cancer clinical trials were opened. The recruitment to existing clinical trials was suspended and screening procedures for eligible patients for possible participation in trials was stopped. Collaborative laboratory centres across Europe were closed and unable to accept trial tissue samples for analysis. There were concerns local radiology services would be limited and our laboratory would be overwhelmed with COVID related samples and unable to prepare samples as indicated by various trial protocols. Clinical trial nursing staff were re-deployed within the hospital to help with demands of COVID-19-related care. A skeleton staff remained in place to oversee the treatment and follow up of patients enrolled already to clinical trials.

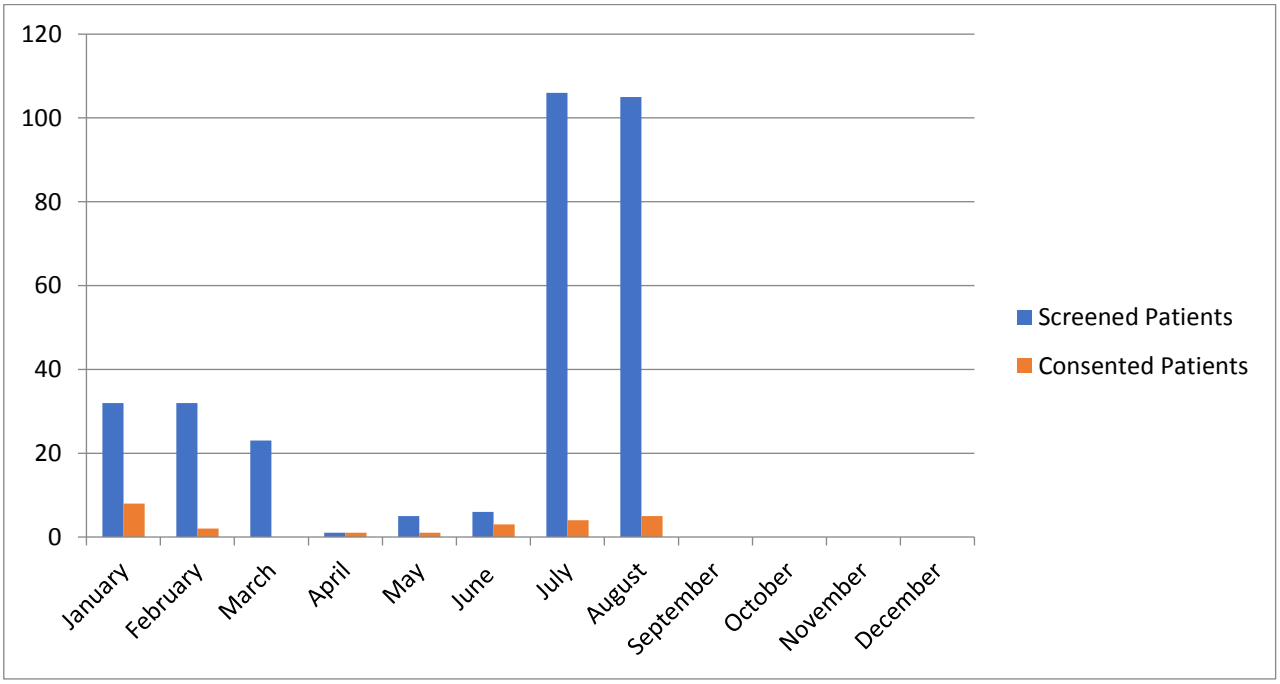
Our statistics illustrate a negative impact in recruitment and screening since the COVID-19 pandemic emerged in Ireland. The smaller number of newly opened trials and the reduction of staffing levels within the CCTU has affected access to new treatments for cancer patients within our region.

In the time period from January 2019 until December 2019, 376 patients were screened for inclusion to participate and 49 (13%) patients signed informed consent to participate in a clinical trial within CCTU at UHL.

In the six months from January 2020 until the end of June 2020, 99 patients were screened and only 15 (15.2%) signed informed consent to participate in a clinical trial (Figure 2 and 3). When these figures are directly compared with the first six months of 2019 there is a 33% reduction in patients screened for participation (147 V's 99) and a 60% reduction in patients consented (37 V's 15) to clinical trials. These figures highlight the immediate negative impact of the global COVID-19 pandemic on cancer clinical trial opportunities and recruitment in our region.



Patients Screened and Consented in 2019 (Figure 2)



Patients Screened and Consented in 2020 (Figure 3)

In July and August 2020 Irish healthcare services attempted to return to a "new normal" due to the dropping numbers of COVID-19 positive patients. During these months of still limited clinical activity across the country, we saw an increase in the number of patients screened for trial participation and a small number of patients signed an informed consent to participate (Figures 2 and 3). Currently there are number of clinical trials due to open, however, as Ireland enters a second surge of COVID-19 cases and further lockdown restrictions are implemented, the future of our practice is uncertain. It is likely that without a national implementation of strategic planning addressing the activity of cancer trial units, recruitment could be further suspended and halted as the health service struggles and staff focus on delivering only essential care.

Learning from the pandemic going forward

Despite the challenges regarding the logistics of clinical trials activity during the COVID-19 pandemic, numerous opportunities to improve clinical trials are identified. Impressive solutions have been suggested and future implementation of these may provide the answers to sustain and support cancer clinical research during the ongoing pandemic. These suggestions include protocol amendments, allowing more flexibility of assessments without hampering treatment safety and efficacy, transfer of cancer research to specific "COVID free" centres for administration of treatment, and telehealth visits for participants, remote site initiation visits and remote consenting as well as the opportunity to ship oral drugs directly to patients avoiding hospital visits where possible [10, 13, 14]. All these changes protect our vulnerable patients while minimising their encounters with possible virus carriers while continuing access to fundamental treatment opportunities. These solutions require investment and may make cancer clinical trials more efficient and patient centred.

The global COVID-19 pandemic has resulted in implementation of novel procedures within clinical research as well as in developing treatments, diagnostics and vaccines to fight the pandemic. The rapid design and launch of these clinical trials, with over 2000 active trials currently in operation, has shown that certain aspects of cancer clinical trials including speedy protocol development and ethical approval approaches could be improved, streamlined and modernised in ways that would benefit patients, clinicians and all researchers [13 - 15].

Conclusion

The COVID-19 global pandemic is continuously evolving. As we enter uncertain times for cancer patients and all involved in their care, it is crucial that we continue to monitor and identify effective strategies to navigate the ever-changing situation. Patient safety and the safety of the staff is the most important consideration going forward but without losing out on fundamental high-quality cancer clinical trial opportunities. This has been an opportunity for deep reflection and to review our practice making permanent adaptions into the future, improving clinical trials and producing a robust evidence base for the treatment of cancer into the future.

Declaration of Conflicts of Interest:
The authors declare no conflicts of interest.

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