Cancerworld

A silver lining: Could changes forced by the pandemic point to better ways to conduct our clinical trials?

Janet Fricker / 23 October 2020

Pragmatic adjustments to trial protocols were seen to be essential during the Covid-19 pandemic to avoid trials being abandoned or delayed. Most changes involved reducing the requirements for travelling to centralised trials centres and reducing the level of reporting requirements. These measures were agreed between trial sponsors, regulators, contract research organisations (CROs) and trial centres as acceptable compromises in the face of unforeseen and unprecedented circumstances. And many clinicians and patients found the reduced demands for travel and reporting made their lives a lot easier.

The changes were made to reduce the risk to patients of exposure to the Covid-19 and minimise opportunities to spread the virus. However, the question now arises: could embracing these changes as standard practice help expand the number of cancer clinical trials and the rate of enrolment, by reducing the burden on trials centres and patients, without compromising the safety of patients or the credibility of the trial results?

In a viewpoint piece published in *JAMA Oncology* in August, under the title ‘Rethinking Clinical Trials Reform During the COVID-19 Pandemic’, three US-based authors argue that they could, and they make the case for grabbing the opportunity offered by the pandemic to take a critical look at how clinical trials are conducted.

They argue that, despite only one in 10 adult cancer patients being enrolled in clinical trials across the USA, steady reductions in cancer death rates since the early 1990s have saved almost 3 million people from dying early from cancer. “One can only imagine the magnitude of benefit that patients would experience if we improve and accelerate clinical trial enrolment,” they say.

They propose six areas where reforms could be made. These cover greater use of telemedicine and virtual platforms, greater use of local laboratories, reduction in the administrative burden, the relative emphasis placed on progression-free survival (PFS) endpoints and patient reported outcomes (PROs), and validation in a real world setting of changes to the way clinical trials are conducted.

Cancer World asked three European cancer trialists and two leading cancer patient advocates what they thought about the changes argued for in the *JAMA Oncology* article:

Point 1: Greater use of telemedicine and virtual platforms

Pre-Covid: Clinical trials were often only available at academic medical centres and frequently required face-to-face visits, which sometimes presented barriers to participation owing to patient out-of-pocket expenses, and the need to travel long distances to centres.

Proposed changes: The introduction of virtual platforms would limit in-person visits only to those that are necessary, and hopefully lead to increased participation in clinical trials. The COVID-19 pandemic has led to the widespread adoption of telemedicine and virtual visits to minimise the risk of to patients of unnecessary exposure.

Point 2: Use of local laboratories

Pre-Covid: Many centres did not allow laboratory studies or procedures to be performed outside of centres where the trial was being conducted, even if patients lived far away and facilities were available locally for laboratory studies or procedures.

Proposed changes: The pandemic has resulted in some sponsors and regulatory bodies being more flexible and agreeing to tests being performed locally and less frequently. The JAMA Viewpoint says there is no reason why routine and basic tests should not be performed at locations convenient to patients, provided no special expertise is needed.

Point 3: Reduction of administrative burden

Pre-Covid: The burden of administrative tasks required by Contract Research Organisations (CROs) from investigators limited the number of patients who could be enrolled into studies and the capacity of investigators to open additional study sites.

Proposed changes: Owing to research site restrictions during the pandemic, CROs were forced to be on site less frequently, and use remote monitoring to ensure quality of collected data. Additionally, some organisations relaxed the need for timely data entry and protocol deviations. Clinical trials exploring vaccines or anti-Covid-19 therapies started recruitment in record times. This process could be applied to cancer trials, especially those recruiting critically ill patients.

Point 4: Reduced emphasis on PFS as an endpoint

Pre-Covid: Driven by the use of progression-free survival (PFS) as the primary endpoint, most clinical trials required frequent imaging studies for assessment of disease status.

Proposed-changes: In the era of Covid-19, even for patients receiving antineoplastic therapies, imaging studies have been delayed. Emerging guidance from the FDA suggests tumour assessments (when appropriate) may be delayed for ongoing trials. Decreasing the frequency of imaging has the advantage of exposing patients to less radiation and iodine contrast, and generating cost savings. However, PFS as an endpoint is heavily dependent on frequent imaging assessments. A way forward, suggest the authors, is to increase the time between imaging studies so that fewer studies are undertaken over the course of the trial, and to use overall survival as the primary endpoint.

Point 5: Increased use of patient reported outcomes

Pre-Covid: Imaging studies were used to make decisions on whether to continue or discontinue individual patients on treatment regimens.

Proposed changes: In the absence of frequent imaging studies, oncologists have redefined 'clinical stability' in terms of how the patient feels. In addition to using efficacy, the JAMA Oncology article proposes that investigators should continue to add patient-reported outcomes (PROs) as another endpoint in future studies. This, they argue, is because these measures have inherent value to patients.

Point 6: Real world evidence studies to test whether Covid trial changes are beneficial

Finally, the JAMA Viewpoint points out that the pandemic offers a great opportunity to use real world evidence to 'pragmatically' test whether changes to clinical trials implemented during the pandemic proved detrimental or helpful to patient care. The authors cite the example of the Covid-19 and Cancer Consortium (CCC-19), which aims to collect and analyse observational data at scale (through crowd sourcing) to inform clinical practice in real time.

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