Realizing the potential of decentralized clinical trials in oncology

Summary

Oncology trials are often multi-site, multicountry large-scale endeavors, requiring collection of a wide range of data from participants. Traditionally, oncology trials have only been carried out at specialist hospitals with the infrastructure to support patients receiving experimental treatments. But with technological and logistical advances, there is opportunity to decentralize some of the components of an oncology trial. This decentralization can boost recruitment of eligible participants, improve patient experience and reduce burden on them and family members for ongoing participation. In turn, this supports patient retention and can improve trial efficiencies through the flow and review of near real-time participant data. In this article, we look at the key tools, technologies and processes that support real-time data review and facilitate more efficient clinical decision-making.

KEY TAKEAWAYS

Many cancer patients are willing to participate in a trial, but fewer than one in 10 actually do

One barrier to participation is the complexity of oncology trials: most require the collection of patient data at frequent intervals—from scans to blood tests, to vital signs and symptoms

Oncology trials have traditionally needed to be carried out at specialized hospital sites, meaning not all eligible patients could take part

Decentralizing components of a trial can overcome these challenges and reduce the burden of participation, boosting the recruitment of eligible patients

Why decentralize oncology trials?

Cancer is the second leading cause of death globally, accounting for nearly 10 million deaths in 2020.[1] The urgency of developing new cancer treatments is reflected by the number of clinical trials in this area, as some 87,000 oncology trials were registered with ClinicalTrials.gov as of October 2019. Despite this, fewer than 5% of patients participate in trials in the U.S.,[2] even though a majority of cancer patients say they are willing to take part in trials. One of the challenges of delivering oncology trials is their complexity. They might involve experimental biological therapies or treatment combinations that require close patient supervision and/or require patients to have their treatment at a specialist clinical center. They also require the collection of a diverse range of patient data at frequent intervals—from scans to blood tests, to vital signs and symptoms. For these reasons, oncology trials have traditionally needed to be carried out at specialized hospital sites, meaning not all eligible patients could take part. Additionally, there has been a considerable burden on the healthcare professionals and resources of study teams running the trials.

One new approach is to decentralize some or all aspects of the trial. New tools and technologies now enable participants to take part in studies from their homes, and data can be collected at locations other than the traditional clinical research site. This model is known as a decentralized clinical trial (DCT) as well as direct-to-patient, remote or virtual clinical trial. However, the multidisciplinary nature, complexity and need for frequent assessments on oncology trials might require a hybrid approach, where patients still travel to the clinical research site for some aspects of their care.

In addition to extending the reach of oncology trials to patients who otherwise might not have been practically able to participate, DCTs or hybrid trials also offer many benefits to sponsors and study teams through the technological components used. Perhaps the greatest added value of a DCT is near real-time data becoming available when participants are supported with technologies that facilitate frequent and accurate data capture. When combined with data management tools such as centralized medical review and reporting, the technological components of DCTs enhance patient surveillance, accelerate data access to the sponsor and create efficiencies in the clinical oversight process, enabling earlier detection and mitigation of study risks.

How decentralized oncology trials work

DCTs allow data collection at locations other than a clinical study site. This might include technologies used by participants themselves: remote monitoring devices such as wearables, mobile apps for electronic patient-reported outcomes (ePRO), and wireless tools such as electrocardiogram or temperature monitors. It may also include remote services such as telemedicine/televisits, direct-to-home medicine supply, direct-to-home sampling and nursing provided at home or through satellite facilities such as primary care or pharmacies. These services can be combined with concierge services to support less abled patients when required to return to the hospital, ensuring continued equity of access and trial participation.

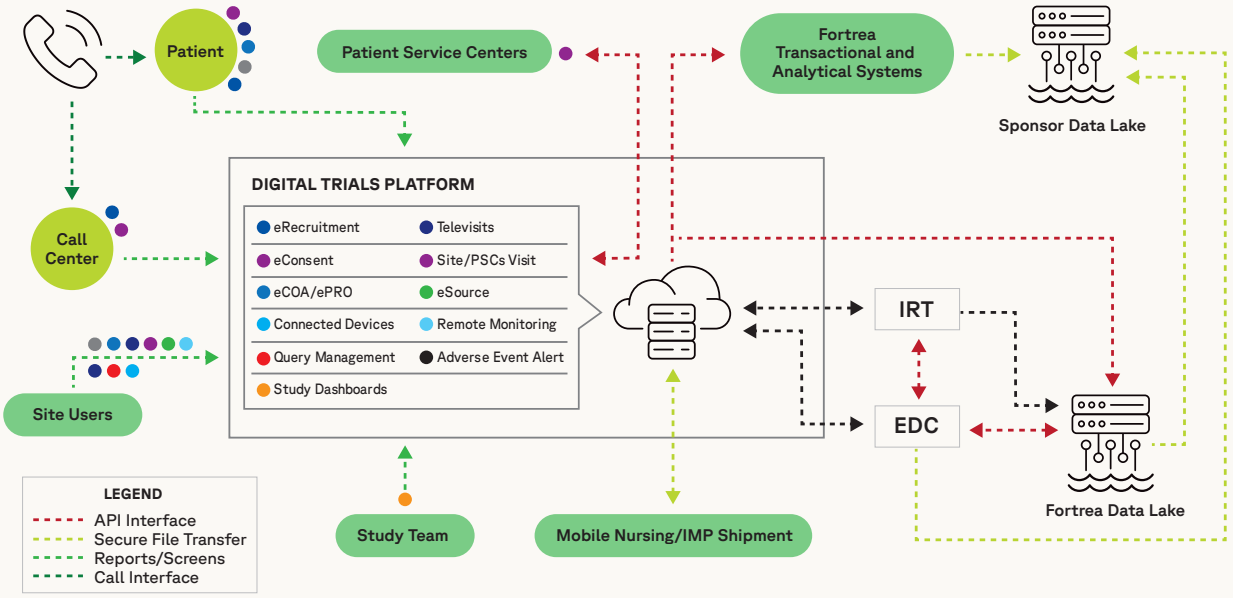
All these DCT components generate a wealth of data and insights that flow from patients and community healthcare professionals to the study teams and sponsor. This provides an opportunity to review, report and act on trial data from disparate sites and within faster timescales than previously possible with conventional centralized studies. For example, centralized review of lab measurements such as liver function has the potential to flag both individual patient-level issues with a trial medicine and broader study-level trends in toxicity. To realize the potential of this continuous data flow, you need a robust digital platform that can integrate data from all sources (e.g., electronic data capture [EDC] database, patient ePRO, televisits and connected devices).

Setting up real-time data flow for your DCT

With DCT technologies, data flows from multiple sources in real time, leading to a continuous clinical data flow that facilitates real-time data access and review. This improves efficiency in monitoring safety and performing clinical oversight, but the data flow pathways need to be carefully configured for each study to optimize data review.

The below diagram illustrates a typical data flow architecture for an oncology trial, run by Fortrea, with the digital trials platform at the heart of the workflow, supported by a state-of-the-art clinical data warehouse and analytical systems that allow review and reporting.

Current Generation Connectivity of Digital Solutions



To establish a DCT data architecture, a robust digital platform needs to be set up that facilitates data flow from EDC platforms through to centralized data review and reporting tools.

The configuration of this data flow architecture should be defined by the unique data flow pathways of each individual study or program and the desired levels of monitoring required by the sponsor. This requires engagement among stakeholders, namely, the sponsor, biometrics team, project management team, lead project physician and medical data reviewer to define critical data parameters and their flow through the DCT platform and determine the appropriate level of monitoring. This includes:

- Understanding and/or discussing critical variables for safety and efficacy based on the trial's study design and phase
- Customizing review requirements rather than performing reviews on predefined patterns for other studies

The Fortrea snapClinical™ digital trials platform is a no-code, drag-and-drop platform of highly tailored, internationally compliant clinical applications that can be set up within weeks. Data (based on the protocol and stakeholder requirements) are then fed into Fortrea's proprietary Xcellerate® Medical Review platform, enabling real-time oversight of pivotal participant-, site- and country-level trial data.

Achieving real-time oversight of study data

The comprehensive review strategy that provides real-time oversight of participant data is carried out by medical data reviewers who work closely with the trial's medical monitors.

The Centralized Medical Data Review (CMR) process starts with entry of the first participant's data into the EDC database. Importantly, the review process is independent of source data verification (SDV) review and other data management activities. This means that clinical research associates (CRAs) can focus their resources on SDV data points not related to medical data. Indeed, the CMR team reduces the SDV burden significantly through centralized review because every participant is reviewed for eligibility as part of the CMR process.

The CMR process consists of the following three tiers of comprehensive data cleaning and review. The exact critical data to be monitored and the frequency are identified through upfront evaluation of the protocol and potential risks that may impact patient safety and study integrity. These are translated into a data review strategy.

Components of a CMR process:

- **Holistic patient review** provides insights on individual participants, providing early detection of safety issues and protocol deviation. These include ongoing eligibility checks, safety and efficacy review including adverse events (AEs) and serious adverse events (SAEs), concomitant medicines and lab tests. These ongoing real-time reviews based on each participant's visit can be customized to the study needs, such as being carried out weekly
- **Aggregate medical review** is the frequency-based review of clinical data across all participants, sites and countries to identify critical trends in AEs, SAEs, lab data and vital signs, plus data inconsistencies that may impact study reliability. This review is monthly but can be adjusted to study needs
- **Medical analytics** provide statistically relevant insights for medical monitors to detect non-random data anomalies that may indicate protocol deviations, bias or other quality issues. It can also detect study-specific analytics such as safety trending, missing data, trends over time and repeating values. This is usually carried out monthly but can be customized to quarterly based on study requirements

The benefits of the CMR process include early detection of critical safety or efficacy signals, insights on key participant-related issues ahead of on-site or remote touchpoints for healthcare professionals, improvement in quality and timeliness of data flow, and optimization of resources (medical monitors spending less time data cleaning and CRAs experiencing lower burden regarding site SDV). Medical analytics also provide oversight and transparency to medical monitors and help with feedback and discussion with trial stakeholders.

A key aspect of realizing the potential of this comprehensive review is to couple it with intelligent informatics-driven reporting tools and technologies. Fortrea's proprietary Xcellerate Medical Review tool not only supports efficient centralized review but also provides visualization tools for enhancing reporting to different trial teams. Various data sources can be integrated in Xcellerate to allow trial teams to review all forms and all the patient data on a single platform, ultimately increasing productivity.

Visualizing and reporting real-time data

The Xcellerate Medical Review tool was developed in partnership with Fortrea's medical monitoring team to meet medical review process requirements. In addition to enabling real-time data review, it provides data visualization tools that can be configured for individual studies. Xcellerate offers the potential to:

- Survey patient data, visualize patterns and outliers, explore aggregate data, and record and communicate notable trends or observations systematically and quickly

- Quickly and easily create interactive and intuitive data visualizations tailored to clinical or safety teams. With a single click, you can access source patient data, making it possible to explore points of interest

- Create or highlight arbitrary cohorts, look at site- or country-level trends or get a longitudinal view of individual patients' or subgroups' progress on the study

- Capture observations and escalate as issues to the Xcellerate Risk and Issue Management application, automatically creating a clear audit trail

- Allow groups of stakeholders to view and discuss observations no matter where in the world they are. Users have the option to create custom views or enhance default visualizations as required

Given that many oncology trials are now large-scale, international endeavors, the extensive reporting and collaborative review capabilities of Xcellerate not only provide a smooth user experience but can improve the reliability of investigational data and ensure adherence to good clinical practice and ethical standards.

Summary

DCTs or hybrid clinical trials are options for expanding the reach and patient centricity of oncology trials. The tools, technologies and processes that support delivery of DCTs facilitate recruitment of more eligible patients and support better retention through to follow-up. Additionally, the components that enable DCTs can also improve trial efficiency by accelerating patient data collection and strengthening trial oversight and patient safety through comprehensive review processes. The real-time nature and frequency of data signals generated from connected devices make it easier to enable early detection in changes to patient behavior or status.

To fully realize these efficiencies in oncology trials, it is essential to configure the data flow architecture and supporting tools, technologies and processes in a way that is appropriate to each study and determined by cross-team collaboration.

This includes establishing a dedicated digital trials platform linked to a customized centralized medical review process and integrated with a tailored reporting tool that provides the right insights to the right stakeholders at the right time.

With these tools, technologies and processes in place, studies will be better aligned to protocol requirements, and clinical study decision-making becomes more efficient.

References

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