Ticking Boxes

Following the guidelines for best practices within immuno-oncology trials can be made easier by following this comprehensive checklist

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With the advent of novel immuno-therapeutic approaches to cancer, the world has entered a new stage of medicine. Rather than targeting cancer cells directly with traditional tools like chemotherapy or radiation, immunotherapy seeks ways to use the body's own immune system to eradicate or inhibit the growth of cancers.

The field of immuno-oncology (IO) focuses on determining how to activate pre-existing immune cells to attack cancerous targets. Monoclonal antibody therapies have shown to be successful in many indications and continue to be an effective and viable approach to treating cancer. According to Beth Kiernan, pharmaceutical research analyst at Thomson Reuters, therapeutic cancer vaccines currently comprise 14% of IO clinical trials (1). Although many vaccine trials are in early stages, advancement has been made into later stages, showing potential for desirable outcomes using this strategy.

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Perhaps the most groundbreaking and rapidly expanding modality of IO is the development of the utilisation of checkpoint inhibitors. Though the industry is just scratching the surface of its promise, checkpoint inhibitors have profound implications on the future of oncological therapies, revolutionising the research industry. Checkpoint inhibitor therapies are able to span across cancer types and stages, providing hope even in the most despairing of circumstances.

Because of its promising outcomes, IO is a significant and growing segment of clinical research, but one that does not come without challenges. Aside from the R&D of these therapies, identifying the most efficacious treatment regimen for each indication poses numerous challenges. As a result, combination studies have increased dramatically, as have the volume of studies, due to the potential of efficacy of one therapy in multiple indications. Studies have become fast-paced and complex, requiring appropriate support from the beginning to the very end of all studies, as the race to the market and the race to save lives is in the balance.

Significant Research Complexities

IO studies pose a significant set of operational challenges for clinical research companies and their development teams. These trials often comprise complex and adaptive study designs that require the collection of multiple specimen types as well as specialised testing on different platforms, such as flow cytometry, genomics, and antibody testing. Due to analytical complexity, studies often require the utilisation of multiple specialty laboratories, which – combined with tight turnaround timelines, the need to maintain specimen integrity, and the need for sites that are geographically diverse – can lead to many logistical challenges. It is not uncommon for development teams to be utilising multiple specialty laboratories that – depending on the study – may be in different countries or even regions of the world, additionally complicating customs and regulatory compliance.

To maintain control of specimen logistics, IO studies benefit from sophisticated sample tracking systems combining point-of-collection accessioning and global tracking with condition monitoring. In this way, study managers can accurately track individual samples from collection through testing and/or processing and then to the sponsor for further study or into a biorepository for secure storage. In IO studies in particular, recognising the value of biological samples and guaranteeing the integrity and ready retrievability of each sample is imperative. Finally, development teams must find new ways to collect, organise, and analyse the staggering volume of data produced during IO trials. Not only must speciality lab data be integrated from multiple, disparate lab datasets, it must be available in real time for safety and efficacy assessments and be able to be visualised graphically to discover anomalies and trends that might otherwise go unnoticed.

Best Practices Checklist

Handling the central and specialised lab requirements is a significant project management challenge in IO research, and it is one that is often augmented by specialised personnel or outsourced entirely. The following is a checklist of best practices for sample and lab

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management to ensure the success of IO studies.

Dedicated Project Management
IO trials have too many moving parts not to have an operational and scientific support team dedicated to handling the testing, sample management, logistics, and lab oversight aspects of a study. Dedicated project managers with experience in logistically complex IO trials and scientific project managers with platform-specific experience for lab oversight can use their knowledge to streamline test schedules and improve efficiencies, as well as oversee vendors, individual labs, and assays to ensure testing is being done properly.

Specialised Testing Experience
In addition to standard safety tests, IO studies require specialised testing capabilities that are not likely to be available in local or even regional labs. Common platforms and procedures include the following:

- Flow cytometry
- Cytotoxic T-cell assays
- Cytokine/chemokine assays and profiling
- IF/IHC
- ELISA
- ELISPOT
- PBMC processing
- RNA/DNA extraction

Sample Management, Tracking, and Logistics
To be research-viable, IO sample logistics must be tightly controlled from sample collection, to transport, to eventual processing, analysis, and storage. Chief among the best practices to preserve sample and data integrity is the development of a comprehensive logistics plan before the trial begins by identifying the labs, procedures, and couriers necessary to a successful outcome. Virtual accessioning of each sample at the time of collection and monitoring the location and condition of each one during transport are vital to maintaining the integrity of the sample and the study.

Data Integration
Reliable lab data is essential in clinical research. In IO trials, this is further complicated by the frequent utilisation of numerous speciality labs to support their analytical requirements. The clinical data integration process involves developing an infrastructure and coordinating programming, coding, cleaning, and conditioning data that may come from a variety of platforms. Only by mapping sources, standardising formats, and merging data can programmers achieve needed data consistency, accuracy, and usability.

BioVisualisation
When sample management and integrated data management are combined with data visualisation programmes, complex data becomes more accessible, understandable, and usable. Data visualisation programmes enable researchers to query clinical sample databases in real time, facilitate diverse, intuitive views of the most current information, and provide alert flagging for critical sample analytes.

Study-Specific Clinical Supplies
Consistency is key in IO trials, and one of the best ways to maximise the value of samples and data collected from a range of different investigator sites is to standardise clinical supplies and collection procedures. It is important to make sure sites are supplied with customised and standardised collection kits that are easy to use, with all the components clearly labelled for the specific collection programme for which it is intended. Kits should also include detailed sample collection and transport instructions and contain preformatted air bills to appropriate labs to save time and reduce the risk of error.

Biorepository
After analysis, samples must be maintained in varying storage temperatures on a short- or long-term basis both as insurance against possible regulatory inquiries and as vital keys to future research. After initial testing and analysis, samples should be secured in a state-of-the-art biorepository that is constantly monitored to ensure sample integrity and that is tightly controlled so that both samples and their annotated data are always accessible for prompt retrieval and shipment.

Global Presence
Owing, in part, to a shortage of patients for clinical trials, IO studies are increasingly global, with many taking place in multiple regions of the world. Because of complications with sample stability and turnaround time, logistics are simplified when the lab is in relative proximity to the investigator site. Depending on the size and scope of the study, an outsourced partner with access to a network of labs around the world and an understanding of country-specific requirements can streamline studies.

Future Outlook

With its new potential to make a significant difference in patients' lives, IO research is poised for continued growth. New methods of action will come to light, and personalised therapies will become a standard of care.

All indications are that IO trials will become even faster paced, more complex, and data-centric in the future. To accommodate the unique needs of these studies, development teams are best served when they identify and partner with central lab and clinical development specialists who can provide comprehensive operational and scientific guidance during the time that protocols are being developed.

Reference

1. *Visit: www.stateofinnovation.com/clinical-trends-and-challenges-in-immuno-oncology*

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