Data and analysis now lead the way

Oncology trials are on the cusp of a technological shift that should make them faster and more streamlined. Caroline Morgan, vice-president of strategic consulting at **Cytel**, talks about the bespoke solutions that align clinical trial data with biometrics, and other new approaches that are helping to lead that change.

What does it mean to have a data strategy that takes biometrics into consideration?

Caroline Morgan: In some companies, clinical operations, including data management and outsourcing, are considered a completely different area of delivery than the statistical discussions that go into clinical trial design or the analysis of clinical data. Unfortunately, this siloed approach can sometimes slow down clinical trials. Particularly in oncology, where we can imagine very complex designs and analyses – the way in which we store, evaluate and aggregate data plays a huge role in how quickly and efficiently we can present it to regulators. Having statisticians on hand who understand the complexity of data logistics, or clinical operations specialists who can anticipate how statisticians might need data stored and presented, creates undeniable efficiencies.

New early-phase designs – like i3+3, MUCE and Bayesian designs – are the talk of oncology right now. What, if anything, do clinical operations and data management teams need to know about this?

A lot of the early-phase oncology designs are aiming to make trials more flexible. This means that statisticians will want to analyse data more frequently. At the same time, one of the goals of the designs is to accelerate clinical trials, so having quick access to data becomes even more important. At Cytel, our statistical programmers have created apps in R Shiny that aim to make data access more user-friendly. These include easy-to-use tables and graphical representations at patient level, population level and beyond.

As an industry we have been thinking a lot about how data are used on a day-to-day basis, and for an oncology trial, like in any trial, it is important to create programmes that support those initiatives. An understanding of how clinical operations work within the context of a specific therapeutic area is therefore key.

How can data strategies be planned for the innovative designs seen in oncology, such as adaptive enrichment or platform trials? What are some questions sponsors should be asking?

This is an important question, but one that highlights the need for bespoke solutions. The kinds of statistical designs we are seeing vary a lot. Cytel's Solara Software, for example, can take the specific commercial needs of a sponsor and design over 100,000 oncology trials for that one situation. It can do all of this in less than 30 minutes, allowing the sponsor to work in real time with the different stakeholders and make an informed decision about the most appropriate design for its particular situation. Understanding the data strategy implications for the chosen design and planning accordingly is key.

You asked specifically about adaptive enrichment designs and platform trials. An adaptive enrichment design first separates an enrolled population based on a specific characteristic, and then decides, after one or more interim looks, whether to move on with the whole population or only a subpopulation, based on a variety of factors. From a clinical operations perspective, we might need to ask ourselves whether there is anything in how we are collecting data or storing data that might make it difficult to separate these subpopulations when needed. We might need to

reinvestigate target enrolments for each of these subpopulations. There are a host of challenges that may come up – some specific to each trial – and experience managing different kinds of trials and identifying opportunities is critical.

A platform trial has treatment arms that are being added or dropped along the way. Optimising the logistics for such trials can present different types of challenges that must be addressed. Also, understanding the specific needs of each stakeholder, including statisticians and regulatory and patient access specialists, is vital to defining appropriate data strategies.

Data pooling is becoming more popular in oncology trials. How can data strategies that allow for data pooling be created?

Data pooling is a broad term that may refer to different ways of integrating data that are not collected as part of the trial being conducted. Some of the data may come from historical data sets like electronic health records or claims data. Some may come from real-world data that are being routinely collected by clinicians independently of a patient's inclusion in the trial. Sometimes we may be using data from different clinical trials.

Data pooling is becoming strategically important for oncology trials. It decreases sample sizes, reducing the number of control patients and/or patient burden. Such strategies raise different challenges for clinical operations and data managers to those in more traditional trial settings.

Anyone who has worked with data knows how hard it can be to consolidate different data sets, and to ensure that nothing is lost as we transform how data are presented. It is also critical to define appropriate methods for data analysis and minimise the risk of bias. Precision and conscientiousness are key, as well as an understanding of data science techniques that can be employed. Think of it like a game of chess or a Rubik's cube: there is more than one way to win, but you need a team that has played enough times to understand and address the challenges at any given moment. You need a team that knows data inside and out, how data can be used and how data uses may change.

What do clinical operations and development specialists need to know about data strategy and biomarkers?

One question we always need to think about with biomarkers is how will the data be used subsequently? For example, exploratory biomarker trials might actually identify promising subpopulations that play critical strategic roles later on. When this situation arises, we should consider how we can collect, store and present data for these various modes of inquiry.

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For later phases of an oncology trial, we might also be collecting data that not only has an impact on a given programme, but on subsequent trials as well. Does current data strategy take into account what those needs might be? Our task is both to be very strict and thorough in how data are used, but also to anticipate novel uses. How can we do that?

It is said that most oncology trials are now rare disease trials. How can lessons learned from data strategy in rare diseases be applied to oncology?

That's true. Now that we are fully in the era of statistical genetics and biomarkers, many clinical trials for cancer are more similar to rare disease trials. This means smaller samples used with a greater sense of what is good for patients as well as for medical discovery. It also means more use of historical data to supplement data collected during a trial. In such settings it may be invaluable to work with a team that has a strong grasp of advanced analytics for real-world solutions.

At Cytel, we have teams with extensive experience interacting with the regulators and designing innovative trials using synthetic control arms, head-to-head comparisons and related trial emulation methods. Each of these design types have different regulatory needs and translate to different data strategies throughout the data collection, storage and deployment journey. Getting to grips with these trial designs and their related data needs is precisely why it is necessary to have bespoke solutions utilising decades of expertise.

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