The Changing Face of Oncology Endpoint Monitoring

Oncology trials have always relied on tumour response to gauge the efficacy of the drugs they assess. But in a world of patient-centricity and value-based reimbursement, do these "hard endpoints" offer developers – and regulators – the whole story?

The traditional primary endpoint for an oncology trial is tumour response, with studies focused on quantifiable signs of a shrinking malignancy and disease-free or overall survival.

Many trials use RECIST, or the Response Evaluation Criteria in Solid Tumours, for example. By measuring tumours, via CT, MRI or X-ray at baseline and throughout the study, researchers can obtain objective, definitive data on a patient's response and disease progression.

What this doesn't tell us is how well the drug was tolerated, and whether the patient believed the burden of treatment was worth the result – information that is becoming crucial to developing successful drugs and getting them approved.

Limitations of the Traditional Approach

In 2001, the Institute of Medicine published Crossing the Quality Chasm[1], a seminal report that named patient-centricity as one of the six goals a healthcare system should fulfil in order to deliver quality care. Medicine should revolve around the patient, respect patient preference and put the patient in control.

There is a growing body of evidence[2] that the systematic monitoring of symptoms, as part of routine clinical care, can result in significantly better outcomes and it has become generally accepted that patient reporting can improve communication, drive satisfaction and ease symptom management[3].

This, combined with a shift towards a value-based approach to care and reimbursement, means patient-reported outcome (PRO) measures have never been more important.

Oncology, which has traditionally relied on tumour response, has been slower to include PROs. In fact, between 2010 and 2014, only three of the 40 cancer[4] treatments approved for use in the USA received any PRO-related labelling.

Limitations of Patient-reported Outcome Measures in Oncology

While the benefits of PROs are generally accepted, there is still, in oncology, uncertainty around what to measure and how to collect it.

The US' Food and Drug Administration (FDA) defines a PRO as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else".[5]

To date, PRO-related endpoints in cancer clinical trials have centred around health-related quality of life (HRQoL). While these provide information of value to the clinician, they do not necessarily indicate what is of primary concern to the patient, or tell us how patients manage their cancer, cope with their symptoms or deal with treatment.

The field is also lacking consensus on how best to embrace the opportunities of these "soft" endpoints. A recent study in paediatric oncology[6] identified barriers to implementation in practice, that equally apply to research, which included inadequate time, insufficient staff, logistics, and a lack of financial resources. Another important barrier is tension between different stakeholders. While clinicians worry payors could misinterpret PRO data, those who develop the performance measures have concerns over the quality of data clinicians collect.

The Future of Oncology Endpoints

Whatever the challenge, improving patient-centredness in oncology is growing in focus.

For decades, the scientific community has been on a mission to battle cancer, and, in large parts, it has been successful. People are living longer after a diagnosis of cancer than ever before. It means that today's oncology therapies don't just have to treat cancer, but also offer tangible quality of life benefits.

Regulators and payors want developers to prove not just efficacy, but value of care, and the traditional fee-for-service model is shifting to value-based reimbursement. As such, real-world data on whether today's sophisticated, yet expensive, cancer therapies improve overall quality of life and value of care is in demand. This information can only come from the patients themselves.

The collection of PROs in oncology research, then, offers a "two birds, one stone" solution to future approval considerations as well as a solid step towards the development of patient-centred, value-based cancer treatments.

Joining the Dots: Building the Big Data Picture

Knowing what to collect is the first step. A study in pancreatic cancer[7] identified a battery of meaningful patient-collected data points. These centred on themes including overall general health and physical ability, as well as satisfaction with caregivers, services and care organisations.

Adherence is another important consideration – no matter how efficacious a treatment is, it won't work if patients aren't taking it. Trials can collect endpoints on treatment plans, intentional or unintentional barriers to compliance, as well as a patient's motivation to follow the regimen.

What's more, PROs can inform regulators on patient satisfaction and experience by asking trial participants to comment on the use and effectiveness of, and trust in, new therapies. Looking at unmet needs and treatment preferences, such as side-effect versus symptom burden, is also useful for proving value.

Collecting all this information in a systematic manner, so that it not only informs drug development and boosts patient-centricity but is also robust enough to support the approval process, requires the utilisation of cutting-edge clinical trial technology.

eCOA software can incorporate relevant, validated instruments that collect the right data at the right time, whether that be from patients, clinicians or caregivers.

Daily symptom diaries allow patients to record how they feel at any given time, rather than be expected to remember the good days and the bad at their next appointment. Adherence trackers provide vital information on compliance and motivation issues. Validated PRO information can offer developers deep insights into how their treatments work and impact on the everyday lives of the patients who take them. And it also provides them with the robust evidence of patient-centric value-based care that regulators are increasingly asking for.

Analytics Provide Data Quality Confidence

In CNS studies, sponsors have used cutting-edge software to bring all this information together and utilised data analytics to monitor the quality of both patient- and clinician-reported outcomes. This has given them the oversight they need to ensure the quality of the data collected and that their clinical trials succeed or fail on the merit of the therapy and not the reliability of the data.

There is a huge opportunity here for oncology to follow suit. Gold standard technology providers can ensure data integrity and boost patient engagement across today's increasingly complex, global cancer trials.

They can help researchers to identify and secure validated instruments and design patient-centric protocols, can improve data consistency by ensuring all raters receive gold standard training, and boost data quality with real-time analytics that root out outliers and potential data quality issues as and when they arise.

Integrating systems such as eCOA with eConsent helps to build the strong site-patient relationships that boost engagement, reduces dropouts and delivers meaningful PRO data.

Augmenting Not Replacing Hard Endpoints

Ultimately, embracing "soft" oncology trial endpoints is not about replacing the "hard" measure of tumour response. The ultimate goal of any cancer therapy will always be to shrink or kill malignant tumours.

But by collecting and centralising all available information, from tumour imaging and clinician-assessed response, to caregiver and patient-reported outcomes, sponsors have everything they need to develop patient-centred therapies and get them approved.

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