

The Medicines Company Developed Nimble Protocols to Scale for Global Trials

The Medicines Company (Now Novartis) Applied CTTI's Quality by Design Recommendations

SUMMARY

Although The Medicines Company (which was acquired by Novartis in January 2020) was a small pharma company, it often conducted large global trials. By implementing Quality by Design (QbD) principles as a standard practice for its study teams, The Medicines Company was able to develop a nimble trial design approach that could scale to match the size of the trials it was conducting.

GOAL(S)

The Medicines Company, which was a fairly small organization of around 100 employees, needed a strategy for designing massive, global cardiovascular trials to detect differences between groups. The study team wanted to pilot a new strategy for the ORION-4 trial, a research study that aims to determine if a new cholesterol-lowering injection safely reduces the risk of heart attacks and strokes in people who have already had one of these conditions, or who have had an operation or procedure to unblock their arteries. The study was coordinated by the University of Oxford and co-sponsored by The University of Oxford and The Medicines Company (subsequently Novartis) in collaboration with researchers at the TIMI Study Group at Brigham and Women's Hospital in Boston.

CHALLENGES

Global trials with large populations tend to bring complexity from both a scientific and operational perspective. The Medicines Company needed to develop a nimble quality strategy that it could scale up while also ensuring the approach was risk-based, allowing the small team to actively monitor the critical components of the trials. The ORION-4 study in particular needed quick results with limited funding, and the study team thought that using a conventional study design approach would take twice the time to enroll and three-times the cost to run than what they had allocated in the budget.

SOLUTION(S)

The ORION-4 study team implemented a QbD approach to streamline the trial and help maintain focus on factors with potential to meaningfully impact the study aims. [CTTI's QbD Recommendations](#) helped the team develop the right strategies and actions to reduce unnecessary complexity and keep the trial on budget.

TAKING ACTION

Protocol development for ORION-4 was a collaborative effort between the academic groups at CTSU and the TIMI study Group and The Medicines Company. In alignment with CTTI's recommendations, it involved the whole clinical team, including individuals responsible for design (medical, scientific, or regulatory) as well as data management, safety, drug supply, operations, site managers, etc. The team ensured everyone involved understood the importance of designing trial in the context of quality, critical versus optional components of the protocol, and regulatory requirements. With that in mind, they defined two critical-to-quality (CTQ) factors: 1) recruitment of the right patients given the fact that the population required was known to be difficult to recruit, and 2) managing retention to mitigate patient dropout or noncompliance with the medication.

For the first CTQ factor (recruitment), the study team required sites to create a list of patients they could invite to participate and also used the National Health System's central system (NHS Digital) to identify potential participants. For the second CTQ (retention), the study team developed an Information Technology (IT) system that allowed sites or regional coordinating centers to have a real-time view of missed or late appointments, as well as non-compliance with the medication. They also established a chat function with study coordinators to enable real-time troubleshooting for issues during the trial. The team established a long, two-month run-in period between the first trial visit and the start of the randomized treatment; the rationale was that if patients were still interested in participating after two months, they would more likely stay enrolled for the 5-year duration of the trial. Sites with a good track record of patient retention were subsequently selected for the trial.

To help the team stay focused on what matters to the study, they pressure-tested every suggested component for the protocol with four core questions:

1. Why do we need this component (or do we)?
2. Can we do this in an easier way?
3. What are the drivers of this component?
4. Can we get this information elsewhere?

Continually returning to these questions during multi-stakeholder collaboration helped keep the protocol as streamlined and focused as possible.

IMPACT

Although QbD was already the standard practice for protocol development and execution for both The Medicines Company and Oxford CTSU, the two sponsoring organizations learned from each other's approaches to implementation of QbD principles. ORION-4 is currently still recruiting, but the team has seen a faster-than-expected rate of recruitment and credits the implementation of QbD to the protocol design and execution.

ADVICE

It is critical that a specific QbD strategy is developed for each trial, reflecting its unique challenges (be it in design,

operation, team structure and organization, resources, etc.).

Resisting the urge to heavily formalize the process across an organization can help QbD become a common sense, helpful approach rather than a bureaucratic to-do that may unnecessarily burden teams.

ORGANIZATION

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ORGANIZATION TYPE

Industry
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TOPIC

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