FOCUS ON ADHERENCE TO EMBRACE DCT BENEFITS

Here, Bernard Vrijens, PhD, Chief Executive Officer and Scientific Lead at AARDEX Group, looks at the effect of decentralised clinical trials on medication adherence in clinical studies.

Decentralised clinical trials (DCTs) offer a multitude of benefits, from expanding access to increasing cohort diversity, but they can also serve to compound existing challenges, such as managing medication adherence.

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If the industry intends to squeeze every drop of potential out of these new ways of working, it needs a thorough understanding of the pitfalls as well as the advantages.

THE VALUE OF ADHERENCE

Poor medication adherence during clinical trials is a significant, long-standing problem with worrying, well-documented consequences. Studies have shown, for example, that 50% of patients across all trial phases admit to not following the dosing protocol.[1] This negatively impacts patient outcomes, leads to underestimations of product efficacy and can threaten study success, even to the point of study failure.

The emergence of DCTs has resulted in huge advantages, such as increasing accessibility and diversity, while lowering the patient burden associated with poor recruitment and retention. But it has also compounded the adherence issue.

DCT CHALLENGES

Fewer site visits can sometimes mean weaker clinical staff-patient relationships. This can impact on the patient's engagement with the trial protocol, which is a well-documented factor in poor medicine-taking behaviour.[2,3]

It could be argued that replacing site visits with home visits removes the so-called "white coat effect", which is defined as improved adherence to treatment around the time of clinic visits.

In addition, by facilitating a more diverse population, DCTs may actually reduce the number of adherent patients recruited. Study teams tend to have a selection bias towards those they know to have disciplined medication-taking behaviour, but broader inclusion remits, including the trend towards open recruitment via social media, can remove this site-imposed filter.

It is also worth noting that many commentators believe digitally enabled DCTs will lead to an increase in side-effect reports. The rationale is that many people attending a monthly site visit are likely to forget mild adverse events (AEs), such as nausea or diarrhoea, between visits. By contrast, when people are asked to log their health status daily, via an app, for example, they may be more inclined to report everything. This is invaluable data, of course, but sponsors and contract research organisations (CROs) need to be ready to receive the predicted additional reports and understand how AEs relate to adherence and dosing patterns.

Of course, variability in assessment translates to variability in clinical outcomes, but the move towards increased off-site assessments by a larger number of clinicians has the potential for lower standardisation of clinical evaluations. As such, it has never been more important for sponsors and CROs to understand the spilt between assessment-related and product-exposure-related variability in their trial data.

CONNECT TO ADHERENCE

Despite poor medication adherence during clinical trials being a problem for decades, it continues to be a stubborn challenge. Traditional methods, such as pill counts, blood sampling and healthcare provider

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(HCP)- or self-reporting, are simply not sensitive enough to tackle the problem.

For example, counting returned tablets is easily censored by participants; and it provides but a summary of adherence between site visits, not the overall understanding of treatment initiation and dosing patterns needed to meet the challenges of the DCT era. The same is true of monitoring drug or drug metabolites in blood, urine or hair, due to the white coat adherence affect, and all reports – self, site or HCP – are vulnerable to bias. All in all, these historic approaches tend to generate incomplete or inaccurate data.

Digital monitoring is different. Combining connected drug packaging and powerful data analytics, for example, is objective, precise and, crucially, provides a holistic view of medication-taking behaviour.

Electronic sensors in the packaging, whether it be connected inhaler, capsule bottle or prefilled syringe, records dose administration and other essential information, and automatically transmits it to the study team. A cloud-based platform then uses sophisticated algorithms to analyse medication-taking behaviour and flag any erratic dosing patterns.

This advanced approach is feasible, reliable and easy to implement, but, importantly, it is continuous. Providing an overall, real-time picture of drug-taking behaviour gives researchers all the information needed to make informed decisions.

Importantly, this advanced model of adherence monitoring is evidence-based. Studies have shown, for example, that it is 97% accurate, compared with 60% for pill count, 50% for healthcare professional rating and just 27% for self-report.[4]

RISK/BENEFIT PROFILE

There is no arguing that DCTs have the potential to make clinical research more representative, more efficient and more patient-centric.

But before diving into this new way of working, sponsors and CROs must first ensure they are aware of any potential threats to the collection of quality data and adjust their workflows accordingly.

By focusing on adherence, organisations can be sure they are working with the full data set, regardless of the impact of DCTs on the way studies run and people behave.

ABOUT THE COMPANY

AARDEX Group is a global leader in digital solutions to measure and manage medication adherence. With operations in Belgium, Switzerland and the US, AARDEX develops and markets digital solutions for adherence-enhancing strategies in clinical trials, research settings and professional healthcare systems. AARDEX is the central actor of a complete ecosystem that combines its MEMS® Adherence Software with a wide range of smart packages and devices that measure patient adherence across all routes of drug administration. AARDEX's vision is to continuously innovate in data-driven medication adherence solutions to enhance digital therapeutics and patient empowerment.

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ABOUT THE AUTHOR

Bernard Vrijens, PhD, Chief Executive Officer and Scientific Lead, AARDEX Group and Invited Professor of Biostatistics, Liège University, Belgium, holds a PhD from the Department of Applied Mathematics and Informatics at Ghent University, Belgium. Dr Vrijens currently leads a research programme investigating (a) the most common errors in dosing using a simple but robust taxonomy, (b) particular dosing errors that can jeopardise the efficacy of a drug and (c) the optimal measurement-guided medication management programme that can enhance adherence to medications and maintain long-term persistence. Dr Vrijens is also the co-author of seven book chapters, over 100 peer-reviewed scientific papers and named as inventor on six patents. He is a founding member of the International Society for Medication Adherence (ESPACOMP), and an active member of several EU- and US-funded collaborative projects around the theme of adherence to medications.