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APPLIED CLINICAL TRIALS

CROs Tackle Neurodegenerative Disease Studies

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Applied Clinical Trials

There has been a recent boom in neurodegenerative disease clinical trials over the past several years, particularly studies that focus on Parkinson's, ALS, and Alzheimer's. Despite this growth, the failure of some neurodegenerative disease clinical trials (i.e., Eli Lily's EXPEDITION3 Alzheimer's study failure) have created a sense of uncertainty in the biopharmaceutical industry. Nonetheless, some CROs, such as Synteract, have invested in growing their neurodegenerative disease portfolio of services, as they believe they can overcome therapeutic-specific challenges to make these studies more successful. In this interview, Linda Rawlings, VP of Neurodegenerative Development at Synteract, elaborates on addressing the challenges of neurodegenerative disease clinical trials.

What are the leading challenges for studies in neurodegenerative diseases?

Linda Rawlings

For diseases like Alzheimer's and Parkinson's, one of the biggest challenges is to properly diagnose, as approximately 30% of patients are misdiagnosed. There are a number of diseases that have Parkinsonian symptoms but aren't Parkinson's. For Alzheimer's, pre-symptomatic patients are often very difficult to detect, as patients exhibit symptoms decades after neurons start to die. There are a few accepted biomarkers and tests, like amyloid-beta, which can be detected in the Cerebrospinal Fluid (CSF), but although widely used, are invasive and expensive, especially when used to pre-screen large numbers of potential patients, many of whom will be screen fails—around 40%. Additionally, some patients experiencing memory loss don't go to their general practitioner (GP) because they are too scared and don't want to talk about it. So, we are trying to identify such patients, making it an easy and positive experience for patients to participate in neurodegenerative clinical trials. This can be done by encouraging patients to talk to their GP once they have concerns about their neurodegenerative function. A positive method to enrich the patient population for participation in Alzheimer's studies is to include pre-screening tests into study protocols aimed at looking at cognitive function in a non-invasive way. There are now a number of accepted and validated cognitive tests performed on iPads and handheld devices, and these tests are generally language and cultural neutral, so that they can be used for international studies. By using non-invasive diagnostic techniques, not only can biopharmaceutical companies save costs, but, are also more likely to generate patient interest and therefore participation in their studies

What are some important aspects that can enhance enrollment and data quality in these studies?

We have to make participation in studies as easy as possible for the patients and their caregivers by reducing burden. We should try and simplify our protocols; unsurprisingly many sponsors want to get as many questions answered as possible and that can be a mistake in many ways. Sponsors should avoid overburdening the patients as well as the sites, as it's very difficult to persuade patients and their caregivers, if appropriate, to sign up to studies that can be perceived as onerous. Sponsors should define few, very well-thought-out assessments that make it clear to the patients and sites what the burden is going to be, and recruitment is greatly aided if you activate sites that know their patients. Additionally, involving home-care vendors at the time of planning the study to schedule home visits with qualified nurses instead of making patients and their caregivers turn up at the site for every visit really helps with reducing dropouts. When patients have to come on site, we can make it easier for them by providing concierge services, such as taxi services and travel reimbursement. Care should also be given to schedule appointments at times convenient to the patients and their caregivers. Moreover, I would suggest that there be as few questionnaires and scales as possible, but sometimes a large battery of tests is required; in such cases, it is important to give the patient breaks between assessments, perhaps splitting visits across two days and offering overnight accommodations to facilitate this. We also need to support study sites by identifying raters within the sites and ascertaining that they are qualified and trained, because these assessments contribute towards critical study endpoints; sometimes even subtle changes can make the difference, hence, we want to ensure consistency of quality of delivering the assessment. We also work with companies who send text messages to remind the patients and their caregivers of upcoming appointments and to remind them that they have a questionnaire that they need to complete. These methods help make the trial as easy as possible for patients, while generating good quality data and supporting protocol adherence.

How important is it to establish relationships with organizations that specialize in neurodegenerative diseases?

We have set up a dedicated group to establish and build further on our relationships with sites and patient advocacy networks. We are often interested in patients who are living at home with earlier mild to moderate onset of neurodegenerative disease. Nursing networks provide nurses to go in and do home visits which can be very useful and contribute greatly towards patient retention. We are also working with patient advocacy groups, specialist websites for Alzheimer's and Parkinson's like the Michael J. Fox Foundation. It provides patients and their families with information and equips sites with training kits, as well-motivated patients and well-trained sites result in good outcomes. These organizations also have registries of on-going studies that patients can go into and look at studies in their area. We also partner with specialist central IRB groups that offer consultancy services by identifying people who are therapeutically aligned so that sponsors have access to experts who advise on new techniques and methodologies to simplify trials. For a Parkinson’s, study in which we were involved, we worked with an organization to set up a screening questionnaire in a database to

which we gave investigators access. Investigators went through the questionnaire and assessed whether their patients were eligible. Doing this also helped pick out which exclusion or inclusion criteria might be prohibitive; this approach was seen to be more efficient than implementing a traditional screening log, and had the potential to reduce the number of protocol amendments, which is typically high for neurodegenerative trials.

Can you discuss an operational challenge you overcame with neurodegenerative studies?

We delivered a series of Phase II to III Alzheimer's studies with a sponsor; the nature of these studies was complex and involved many vendors. Additionally, there were numerous blood and CSF tests necessitating multiple labs, which introduced challenges, especially for sites. So, we addressed the

complexities associated with the use of multiple vendors by streamlining operations; we established procedures for the sites to ship basic lab samples to a single receiving lab that would be responsible for processing and shipping samples to various specialty labs. To elaborate, the vendor was in charge of all the processing, splitting the samples, keeping duplicate aliquots, where necessary, and making sure the samples are packaged and stored per the protocol's requirements. This alleviated site burden, contributed to protocol adherence and reduced mistakes.