Challenges for CNS clinical trials - why are there so many failed studies?

The CNS Company’s Project Director, Susan McGoldrick reviews the recent findings on yet more failed trials and offers some hope!

Two recent articles in Lancet Neurology and Nature Reviews Neurology looked at the reasons behind recent clinical trial failures, one article looked at neuroprotective therapies for Parkinson's disease and the other looked at clinical trials in amyotrophic lateral sclerosis. The reasons behind these were surprisingly similar, given one is a serious, common, progressive disease and the other is a rare, often fatal, rapidly progressing disease. Both diseases however share the fact they are caused by degeneration of the brain, although in different parts of the brain. Indeed the entire field of CNS disorders is characterised with failed trials and poorly treated conditions. And the reasons? The first reason in both papers was incomplete knowledge of the biology of the disease. This then leads to a lack of biomarkers, animal models that are not an accurate reflection of the disease and rating scales that are insensitive to detecting change over the time frame required for a clinical trial. These areas coupled with inaccurate diagnosis and the difficulty of achieving a homogenous population within a lot of these CNS diseases have been the lessons learned from these negative clinical trials. There is a huge need for effective medicines to treat patients with CNS disorders. This need often means that there is pressure to move quickly from hypothesis to proof in pivotal clinical trials. However does this mean that we are moving too fast... not fast enough would generally be the cry of patients.

Is there any cause for optimism?

Well some say that the recognition of the problem is the first step to recovery and indeed there is wide spread recognition of the problems with CNS drug trials. So here are some top tips if you are working in this area for your clinical trials:

- Endpoint selection. Know how the endpoint relates to the disease and the timeframe to detect a clinically meaningful change.
- Patient selection, not just diagnosis but remember to consider staging of patients in their disease pathway. Are you sure you are including patients not only with the same disease but are they at the same stage?
- Include a measure of biological activity at the target site within the patient. If you cannot measure this then you need to realise you are working in the dark. These measures could be through imaging, blood/plasma or CSF collection or PK sampling.

It is interesting to note that rare CNS diseases face the same challenges as more common CNS diseases. There is however much more help available to companies working in rare or orphan diseases. Perhaps with this extra help we will see an increase in clinical trials in CNS and the advances in treatment that are so desperately needed.