Identification of Sites of Concern in a Large Parkinson’s Disease (PD) Clinical Trial - Preliminary Findings

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ABSTRACT

Background: A review of the entire population of subjects participating in a PD clinical trial revealed significant opportunities for improvement in data quality assurance and site monitoring. Methods: The automated statistical algorithm identified thirty sites as ‘potentially concerning’. Of these, thirteen sites were identified as ‘concerning’ in more than one aspect. Several sites were identified as ‘concerning’ in more than one aspect. Cosa examples for each site of concern are depicted in Figures 1 to 4. Figure 1 demonstrates an example of a site with data clustering around inclusion criterion at baseline indicating potential score inflation. Figure 2 compares a site with overtly consistent ratings with a site with erratic ratings across visits indicating potential issues in UPDRS administration. Figure 3 shows Figure 4 shows a high responding site, the finding of which may indicate potential selection bias.

RESULTS:

We reviewed 1500 individual subject visits collected from 368 screened subjects at all research sites. The automated statistical algorithm identified thirty sites as ‘potentially concerning’. Of these, thirteen sites were identified as ‘concerning’ in more than one aspect. Several sites were identified as ‘concerning’ in more than one aspect.

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CONCLUSIONS:

Using simple statistical methods followed by clinical review we were able to identify thirteen sites of concern in a large Phase III PD clinical study. This analysis was intended as exploratory as we aimed to investigate the potential for such analysis in PD trials. While this was a single time analysis, a repeated analysis on a predefined frequency would allow identification of questionable sites earlier and facilitate subsequent follow-up actions such as CRA monitoring visit at the site, sponsor audit at the site and retraining of site staff, etc. The main issues identified as source of concern are not unique to PD studies, but have also been identified in other disease areas including schizophrenia, depression or anxiety (Daniel et al, 2008). To our surprise, we identified approximately 10% of subjects with changes in clinical sign laterality between visits. This finding is of particular concern as it implies that approximately 10% of such study data may be questionable or flawed. While many of these laterality changes can likely be explained by transcription errors, many of the reviewed cases did not reflect such a mistake and other reasons for such discrepant data need to be considered including data fabrication.

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