Imaging Biomarkers

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Clinical pharmaceutical trials in neuropsychiatric disorders from Phase 1–4 incorporate multiple outcome measures to assess the safety and efficacy of treatment including clinical observation, rating scales, and physiological evaluations. In particular, the use imaging biomarkers have become an important component of clinical research trials in CNS disorders like Alzheimer’s disease (AD) where they may serve a variety of roles in the clinical investigation including, 1) providing an objective measure of disease or a pathophysiologic process, 2) aiding in diagnosis or disease risk assessment, for enriching enrolling subject cohorts, 3) providing mechanistic information about treatment, 4) monitoring response to treatment and/guide therapy, and 5) offering a surrogate endpoint to substitute for a clinical endpoint.

Yet even as there has been the dissemination of imaging technologies which support the widespread use of imaging biomarkers in large clinical CNS trials, there remain critical problems of technical standardisation, availability of investigational radiotracers, and the logistics of coordinating radiochemistry, imaging, and clinical centers to quantitative, poolable imaging data which meet regulatory standards.

In this regard, there is limited published data, although initial experience suggests PET can successfully serve these multiple roles. This is borne out by the number of new trials utilizing PET biomarkers for different clinical research purposes. Keying off the explosion of studies incorporating 18F amyloid PET biomarkers in AD therapeutic trials, we focus on trends in the use of multicenter PET imaging and key technical issues in the successful design and implementation of such trials.

In conclusion, the widespread incorporation of imaging biomarkers in multicenter trials raises challenges for standardisation of PET for the imaging center, the central core lab, the study sponsor, and the regulatory authorities, which are being evaluated and solved in the course of on-going studies including the creative use of phantoms, rigorous technical set-up and subsequent monitoring of PET studies, and central standardised analysis of imaging data.

References


