U.S. Food and Drug Administration/Center for Drug Evaluation and Research (CDER): Parkinson's Disease Research and Drug Development

With increases in the aging population, the prevalence of neurodegenerative diseases such as Parkinson's disease will increase. Drugs that can slow the worsening of symptoms are clearly needed, but tools to guide the design of clinical trials which can measure the effect of a drug on disease progression are not available. Our research has used existing clinical trial data to develop publicly available quantitative models that may aid in the successful design of clinical trials that support evaluation of the disease modifying potential of newly developed therapies for Parkinson's disease.

Lead Agency:

U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER)

Agency Mission:

The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.

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Partner Agencies:

National Institute of Health
University of Rochester, NY, Parkinson's Study Group
Michael J Fox Foundation for Parkinson's Disease

Parkinson’s Action Network

General Description:

With an increasing aging population, the number of Americans who suffer from neurodegenerative diseases such as Parkinson's disease will increase. Parkinson's disease is a debilitating movement disorder that severely curtails the quality of life for patients and may lead to other serious secondary complications. Available drugs to treat this disease primarily provide symptomatic relief, but do not slow the disease progression. Drugs which may provide symptomatic relief when Parkinson's disease is first diagnosed become less effective as the disease progresses. Pharmaceutical companies are now developing drugs intended to slow the disease progression. Success of these development programs will have a major impact on public health. The scientific challenges associated with drug development programs are paralleled by scientific challenges associated with the development of objective evaluation tools to gauge the effectiveness of disease modifying treatments. Clearly, the trial designs, endpoints and analyses currently used for evaluating the effectiveness of drugs for symptomatic benefit are not applicable for testing whether a drug slows the progression of a disease. Thorough scientific research on the appropriate endpoints for discerning symptomatic and disease modifying effects is imperative if new therapies are to be successfully developed and evaluated.

A group of FDA scientists initiated the Parkinson's disease research project with the goal of developing objective models and tools to aid in the design and evaluation of clinical trials intended to demonstrate a disease-modifying effect. The approach focused on using previously collected clinical trial data to develop a quantitative description of multiple factors important to predicting disease progression in clinical trials. Patient level disease, demographic, trial design and other relevant data from several clinical trials within the FDA files and a NIH sponsored trial were collected and quantitative disease-drug-trial models for Parkinson's disease were developed. These models described the natural progression of the disease, patient disposition in terms of baseline disease severity, patient’s age at disease onset, projected drug effects on disease progression, and reasons for patient discontinuation. Subsequently, the models were employed to explore competing endpoints and analyses that could demonstrate a disease-modifying effect. The results of the research were presented at the FDA Clinical Pharmacology Advisory Committee meeting (October 2006), and later at a public conference sponsored by FDA, Michael J Fox Foundation, Parkinson's Study Group, and American Association of Pharmaceutical Scientists (April 2008).

The generalized mathematical model is a useful tool which may support the effective design of clinical trials by clinical investigators/researchers in the pharmaceutical industry and academia, thus advancing the public health by helping to speed innovations in drug development.

Excellence: What makes this project exceptional?

1. High public health value: Parkinson's disease is debilitating and patients need new therapies that not only provide relief of symptoms, but that retard the rate of disease progression. However, FDA and industry have little experience with drug development programs for drugs with this indication. Clear guidelines on how to develop such drugs and demonstrate disease-modification (i.e., slowing disease worsening) are lacking. FDA took a proactive step in leading the scientific thinking and building knowledge on how to efficiently develop and evaluate such drugs.

2. Objective use of prior knowledge: The first step in developing guidelines for future development is to accrue prior knowledge. FDA scientists evaluated prior trials submitted as part of New Drug Applications and a NIH sponsored study to appreciate the key features of the underlying disease. Specifically, the research set out to answer questions such as: How fast does a patient's disease worsen? What patient characteristics, if any, control the pace of the disease's progression? Do patients discontinue treatments because of toxicity or due to lack of effectiveness? Answering these questions was crucial to explore strategies to test if a new drug indeed modifies the pace of the disease. FDA is in a unique position to address these questions with its access to vast archive of clinical trial data and expertise in pharmacometrics, clinical trial design and biostatistics. Leveraging that knowledge is in the best interest of public health.

3. Effective collaboration across institutions/disciplines towards public health advancement: FDA scientists recognized the need for a collaborative approach to this research. The Offices of Clinical Pharmacology, Biostatistics and New Drugs within FDA collaborated actively in seeking answers to the above questions. At different stages of the research, different organizations/groups were engaged, which included: FDA, Michael J Fox Foundation for Parkinson's Disease, University of Rochester, NY, Parkinson's Study Group, Parkinson's Action Network, several pharmaceutical industry representatives, and FDA advisors.

Significance: How is this research relevant to older persons, populations and/or an aging society?

Parkinson's disease is a debilitating disease, which occurs mostly in the elderly. These aging patients need better drugs, which not only provide relief of symptoms, but retard disease progression.

Effectiveness: What is the impact and/or application of this research to older persons?

Developing guidelines on testing for drugs developed to slow disease progression is important to promote the design of efficient clinical trials that will provide for a clear and objective evaluation of new therapies which seek a disease modifying claim.

Innovativeness: Why is this research exciting and newsworthy?

This is an example of FDA scientists recognizing the tremendous public health benefit that can be realized by proactively leveraging prior knowledge in a systematic manner to aid future drug development. The creativity and dedication of the scientists involved is illustrated by the fact that much of the work was accomplished outside of their regular work assignments. This project exemplifies the tremendous potential of FDA's Critical Path Initiative to improve the public health by providing tools that can reduce the uncertainties surrounding development of urgently needed new therapies.