Background and Objectives

The Critical Path for Parkinson’s (CPP) Consortium, primarily funded by the charity Parkinson’s UK, focuses on developing approaches to designing more efficient clinical trials, based on the combination and analysis of data from thousands of individuals who have participated in clinical studies around the world.

CPP aims to develop a disease progression model that will allow researchers to more reliably predict specific time courses and disease progression patterns, from early motor Parkinson’s disease (PD) to more advance stages. This will be possible by generating mathematical models that will account for the interplay of relevant factors (age, gender, baseline severity, genetics, imaging test, etc.) in driving predictions of disease progression over time. This approach will allow researchers and drug developers to simulate many different combinations of these factors and predict what disease progression patterns will be observed in specific subpopulations. With the information generated by the model, the Parkinson’s field will be able to apply similar modern approaches compared to those that other sectors (aerospace, structural engineering, etc.) readily apply for research and development. A striking example of what model-based drug development could become is how the most efficient launch trajectory for the U.S. Space Shuttle was determined by modeling and simulation approaches that took into account relevant aspects of aerodynamic performance and orbital dynamics. CPP aims to modernize drug development for Parkinson’s by developing similar modeling and simulation strategies for drug development (Figure 1).

![Figure 1](optimized_launch_trajectory_u_s_space_shuttle Derived_from_computer_simulations_V.D._Kern.jpg)

Work Plan

CPP’s modeling and simulation team, led by Drs. Klaus Romero, Timothy Nicholas, Kuenhi Tsai, and Daniela Conrado, will develop the proposed mathematical model and simulation platform, based on the integrated patient-level database that the CPP data team is developing. This database will integrate patient-level data from different observational studies and clinical trials in Parkinson’s disease (Ref. 1) (Figure 2).

With the contributions from CPP’s partners from industry, academia, charities, government agencies and regulators, this quantitative modeling and simulation platform will be then put through a formal regulatory review process at FDA and EMA for its potential endorsement for use in planning of efficient clinical trials (Figure 3).

![Figure 2](maximizing_use_of_exiting_data_to_create_new_clinical_devlopment_tools_RCT_Randomized_Clinical_Trial.jpg)

The modeling and simulation platform will be based on a quantitative disease progression model, which will mathematically describe how the motor signs of PD evolve over time, depending on relevant factors like age, gender, initial severity, status of the dopamine system in the brain (as per molecular imaging), genetics, family history, etc.

Expected Impact

The regulatory evaluation and endorsement of modeling and simulation platforms will provide the necessary confidence for sponsors to make use of CPP’s quantitative drug development platforms to optimize the clinical trial design, and thus achieve a more-efficient drug development process for Parkinson’s disease (Ref. 2). As an example, refining the inclusion criteria based on the model will decrease the likelihood of enrolling individuals with a low probability of benefitting from potential therapeutic candidates. As such, CPP’s approach provides the framework for the adoption of an integrated drug development process, incorporating modeling and simulation platforms as well as biomarkers that provide useful and significant insights into the nature of disease progression in Parkinson’s disease. The current way of designing clinical trials to test potential new drugs for Parkinson’s will be radically transformed once this platform becomes available (Figure 4).

![Figure 4](benefits_of_a_non-traditional_data_and_quantitative_model-based_drug_development_approach.png)

References


(2) FDA’s Critical Path Initiative: [http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/ucm076689.htm](http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/ucm076689.htm)

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