A computational tool to optimize clinical trial parameter selection in Duchenne muscular dystrophy: A practical guide and case studies

Jordan Wilk, Varun Aggarwal, Mike Pauley, Diane Corey, Daniela J. Conrado, Karthik Lingineni, Juan Francisco Morales, Deok Yong Yoon, Yi Zhang, Zihan Cui, Jackson Burton, Jane Larkindale, Shu Chin Ma, Collin Hovinga, Terina Martinez, Klaus Romero, Ramona Belfiore-Oshan, Sarah Kim, the Duchenne Regulatory Science Consortium (D-RSC) and the CINRG DNHS investigators

Abstract

Duchenne muscular dystrophy (DMD), a rare pediatric disease, presents numerous challenges when designing clinical trials, mainly due to the scarcity of available trial participants and the heterogeneity of disease progression. A quantitative clinical trial simulator (CTS) has been developed based on previously published five disease progression models describing each of the longitudinal changes in the velocity at which individuals can complete specified timed functional tests, frequently used as clinical trial efficacy endpoints (supine-stand, 4-stair climb, and 10 m walk/run test or 30-foot walk/run test), as well as each of the longitudinal changes in forced vital capacity and North Star Ambulatory Assessment total score. The model-based CTS allows researchers to optimize the selection of numerous trial parameters for designing trials for the five functional measures commonly used as endpoints in DMD clinical trials. This case report serves as a demonstration of the tool's functionality while providing an easy-to-follow guide for users to reference when preparing simulations of their own design. Two case studies, using input selection based on previous DMD clinical trials, provide realistic examples of how the tool can help optimize clinical trial design without the risk of decreasing statistical significance. This optimization allows researchers to mitigate the risk of designing trials that may be longer, larger, or more inclusive/exclusive than necessary.

Read the publication