CHANGES IN FOUR-STAIR CLIMB (4SC) OVER 2 YEARS IN DUCHENNE MUSCULAR DYSTROPHY (DMD): CHARACTERIZING RATES OF DECLINE AND PROGNOSTIC FACTORS

Goemans N[1], Signorovitch J[2,3], Ong R[4], Rabbia M[5], Dukart J[4], Sajeev G[2], Jenkins M[2], Hossain I[2], Yao Z[2], Ward S[3], for the Collaborative Trajectory Analysis Project (cTAP)

[1]University Hospitals Leuven, Child Neurology, Leuven, Belgium
[2]Analysis Group, Inc., Boston, MA, USA
[3]Collaborative Trajectory Analysis Project, Cambridge, MA, USA
[4] Hoffman-La Roche, Basel, Switzerland
[5]Roche Product Development, Roche Innovation Center New York, New York, NY, USA

Background: Longitudinal statistical models are used to measure drug efficacy in randomized clinical trials or in comparison to natural history controls. To maximize power and validity for measuring drug effects, these models often incorporate knowledge of prognostic factors and typical patterns of change in outcomes over time. To this end, the present study investigated longitudinal models for 2-year changes in the timed four stair climb (4SC) test in DMD patients treated in routine clinical practice.

Methods: Patients in this study were boys with DMD receiving care at UZ Leuven, a pediatric neurology clinic in Belgium, and were aged 6-18 years, receiving systemic corticosteroids for at least 6 months and able to complete the timed 4SC test in 12 seconds or less. Longitudinal models for changes in 4SC velocity were studied, considering different prognostic factors and linear vs. curved patterns of change over time.

Results: A total of 57 boys contributed 101 periods of ~2-year follow-up. At the beginning of these follow-up periods, mean age was 9.4 years; mean 4SC time and velocity were 3.6 seconds and 1.5 stairs/second, respectively. The best-fitting model for 2-year changes in 4SC velocity included multiple baseline prognostic factors (age, 4SC velocity, 10 meter walk/run velocity, rise from supine velocity, deflazacort use, as well as height and weight) and curvilinear (quadratic) patterns of change over time. For the average patient, mean declines in 4SC velocity were 0.09 stairs/second over the first 48 weeks and 0.20 stairs/second over weeks 48-96.

Conclusion: Analyses of 2-year changes in 4SC velocity in DMD should incorporate important baseline prognostic factors, including multiple measures of ambulatory function, and should accommodate the potential for accelerating rates of decline. Models such as those provided here can help detect and measure the effects of new treatments on ambulatory functions in DMD.