

Ralf Reilmann¹, Mark Forrest Gordon², Robin Schubert¹, Karen E. Anderson³, Andrew Feigin⁴, Sarah J. Tabrizi⁵, Blair R. Leavitt⁶, Julie C. Stout⁷, Paola Piccini⁸, Beth Borowsky², Gail Rynkowski², Rita Volkinshtein², Juha-Matti Savola², Michael R. Hayden²

¹George-Huntington-Institute, ²Teva Pharmaceuticals, ³MedStar Georgetown University Hospital & Georgetown University Medical Center, ⁴NYU Langone Health, ⁵University College of London, ⁶University of British Columbia, ⁷Monash University, ⁸Imperial College London

Quantitative Motor (Q-Motor) Assessments Suggest a Beneficial Central Effect of Laquinimod in a Phase II Study in Huntington Disease (LEGATO-HD)

Objective: Evaluate the change from baseline at week 52 in Q-Motor (Quantitative Motor) measures, exploratory, standardized, and rater-independent outcomes in the LEGATO-HD study.

Background: LEGATO-HD assessed laquinimod as treatment for Huntington disease (HD). While the primary endpoint UHDRS-TMS, a categorical rater-dependent scale assessing motor symptoms, did not show changes, the secondary endpoint of benefit in change from baseline in caudate volume was met.

Methods: Q-Motor assessments performed at baseline and weeks 4, 13, 26 and 52 included digitomotography (index finger speeded tapping), dysdiadochomotography (pronation/supination hand tapping), manumotography and choreomotography (grip force and chorea analysis), and pedomotography (foot speeded tapping). Data from 48 sites in 10 countries was transferred online for centralized quality control and automated blinded analysis.

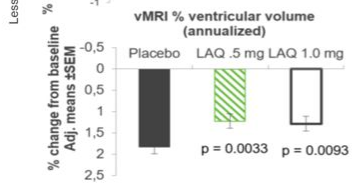
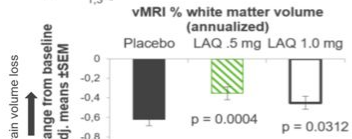
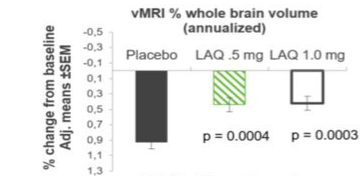
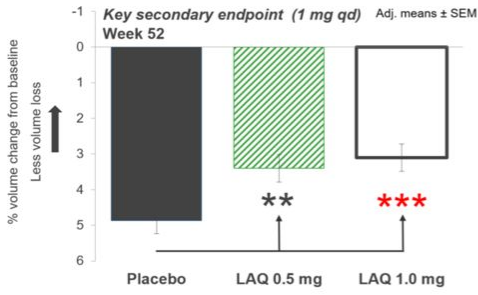
Results: Q-Motor data was collected from 317 patients in the placebo, laquinimod 0.5 mg and 1.0 mg treatment arms. Speeded finger tapping (digitomotography) measures (e.g. frequency, duration and variability of inter-onset intervals, inter-peak-intervals, and inter-tap-intervals) demonstrated improvements with nominal statistical significance ($p < 0.05$) at 0.5mg and generally positive trends at 1mg and is consistent with the reported improvements seen in MRI assessment of brain volume changes (Fig 1). Analysis of pronation/supination (dysdiadochomotography) and foot speeded tapping (pedomotography) in similar parameters to speeded finger tapping showed some positive trends. No relevant changes were seen in grip-force (manumotography) and chorea (choreomotography, i.e., position-index and orientation-index). All measures showed a general worsening in the placebo group.

Conclusions: Q-Motor revealed nominally significant improvements in several tapping measures in the 0.5mg group and positive trends in several parameters for 1mg group, compared to placebo. Similar to previous studies all Q-Motor measures worsened in the placebo group. The results of the Q motor assessment must be viewed cautiously as corrections for multiplicity were not performed on these analyses, however these observations suggest a central beneficial effect of laquinimod in LEGATO-HD of unknown clinical significance and support a biological relevance of the imaging changes observed.

Figure 1. MRI Volume and Q motor assessments in the LEGATO-HD study

MRI volume

% Caudate volume loss / year



Q-Motor



Inter-Onset-Interval (IOI) [right]

