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

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BACKGROUND and OBJECTIVE

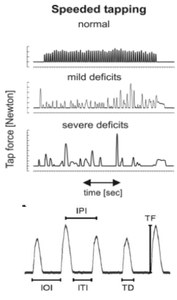
- For patients with Huntington disease (HD), the assessment of motor symptoms in the clinic is often done using the Unified Huntington's Disease Rating Scale-Total Motor Score (UHDRS-TMS), a categorical rater-dependent scale which rates various motor signs including eye movements, speech, chorea, dystonia, rapid alternating movements, bradykinesia and gait.[1]
- Alternatively, motor signs can be objectively and quantitatively assessed in the clinic using sensor-based measures, as in the quantitative motor (Q-Motor) battery applied e.g. in the TRACK-HD and PRIDE-HD studies.[2,3]
- The LEGATO-HD study assessed laquinimod as a treatment for HD. While the study primary endpoint UHDRS-TMS did not show a significant difference between placebo and laquinimod groups, the secondary endpoint was met as there was a significant reduction in caudate volume loss in the laquinimod 1.0 mg group compared to the placebo group.
- The present report describes the assessment of motor symptoms in the LEGATO-HD study using the Q-Motor measures, as an exploratory and rater-independent outcome.

METHODS

- Q-Motor assessments were performed at screening, baseline, and at weeks 4, 13, 26, and 52. The changes from baseline to each visit and to week 52 were analyzed.
- The Q-motor battery consisted of five ambulatory-applied sensor-based assessments:
  - Digimotography (speeded finger tapping) **(Fig. 1** below)
  - Dysdiadochomotography (pronation/supination hand tapping)
  - Manumotography (grip force)
  - Choreomotography (chorea analysis)
  - Pedomotography (speeded foot tapping)
- The data from the sites were transferred online for central quality control and an automated blinded analysis.
- The Q-Motor assessments were defined as exploratory endpoints and the various parameters contained in each type of assessment were analyzed.
  - As these were exploratory analyses, all p-values reported are nominal and have not been corrected for multiplicity.

Fig 1. Digimotography

- Direct physiological readout
- Recognizable “Gestalt” of pathology
- Sensitive 10-20 years before HD manifestation in HD gene carriers



Bechtel, et al. *Neurology* 2010.

RESULTS

Patient Disposition and Demographics

- LEGATO-HD was fully enrolled with 352 patients participating at 48 sites in 10 countries.
- Q-Motor data was collected from 317 patients in the placebo, laquinimod 0.5 mg and 1.0 mg treatment arms.
- Baseline demographics were well balanced across treatment groups. Patients enrolled were in early stage HD.

Table 1. Patient baseline characteristics*

	Placebo (n = 108)	LAQ 0.5 mg (n = 107)	LAQ 1.0 mg (n = 107)
Age, years	43.8 (7.8)	43.3 (7.8)	44.0 (7.8)
Sex, n (%) males	52 (48%)	55 (51%)	53 (50%)
CAG repeats	44.2 (2.4)	44.4 (2.5)	44.0 (2.2)
Months from HD diagnosis	32.3 (31.9)	45.8 (42.0)	41.5 (50.3)
Months from onset of HD symptoms	52.7 (43.6)	60.9 (43.0)	57.8 (51.1)
UHDRS-TMS	26.4 (14.6)	24.0 (13.2)	22.1 (10.7)
Q-motor: Digitomotography Tap-Speed-IOI MN Hand, sec	.335 (0.13)	.330 (0.13)	.311 (0.10)
Q-motor: Digitomotography Tap-Speed-IOI SD Hand, sec	0.113 (0.08)	0.107 (0.07)	0.088 (0.05)
Q-motor: Digitomotography Tap-Speed-IOI SD Hand-R, sec	0.096 (0.07)	0.091 (0.07)	0.077 (0.05)
Q-motor: Digitomotography Tap- Speed-IPI MN Hand, sec	0.335 (0.13)	0.33 (0.13)	0.312 (0.10)
Q-motor: Digitomotography Tap-Speed-IPI SD Hand, sec	0.108 (0.08)	0.104 (0.07)	0.086 (0.05)
Q-motor: Digitomotography Tap-Speed-IPI SD Hand–R, sec	0.093 (0.07)	0.089 (0.07)	0.075 (0.04)
Q-motor: Digitomotography Tap-Speed-Frequency MN Hand, Hz	3.451 (1.1)	3.505 (1.1)	3.579 (0.97)

* IIT cohort, mean (SD) unless otherwise specified; IOI = Inter-Onset-Interval; IPI= Inter-Peak-Interval; MN=mean, SD=Standard Deviation

References

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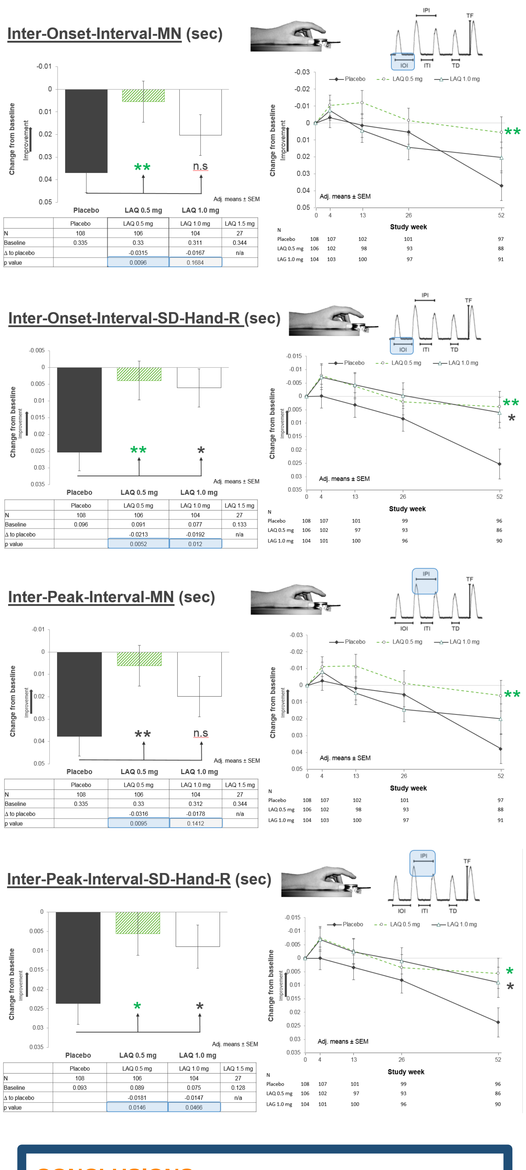
RESULTS

- In most of the Q-motor assessments, there was no significant difference when comparing the laquinimod 0.5 mg and laquinimod 1.0 mg to the placebo group.
- However as shown in **Fig 2**, speeded finger tapping (digitomotography) assessments demonstrated improvements with nominal statistical significance ($p < 0.05$) at laquinimod 0.5 mg and generally positive trends at laquinimod 1.0 mg for duration and variability of the following measures:
  - inter-onset interval (IOI)
  - inter-peak-interval (IPI)

Fig 2. Digitomotography assessment



CONCLUSIONS

- Q-Motor assessments revealed nominally significant improvements in several digitomotography tapping measures in the laquinimod 0.5 mg group and a few in the laquinimod 1.0 mg group, compared to placebo.
- Similar to previous studies all Q-Motor measures worsened in the placebo group, i.e. placebo responses seen in the UHDRS-TMS clinical rating scale were not observed.
- The results of the Q-Motor assessments must be viewed cautiously as corrections for multiplicity were not performed on these analyses.
- However, the consistency of the observations across measures suggests a central beneficial effect of laquinimod in LEGATO-HD of unknown clinical significance.
- These observations support a biological relevance of the MRI imaging changes observed and described in MDS 2019 poster number 43.

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