caused ballismus movements in this case. In patients who present with short duration monoballismus, evaluation for subthalamic nuclei function, seizure disorders and other origins of ballismus are warranted.

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Cardiovascular Safety Assessment of Deutetrabenazine in Healthy Volunteers and Implications for Patients With Huntington Disease or Tardive Dyskinesia

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ABSTRACT: Introduction: Deutetrabenazine is approved for treating Huntington disease (HD) chorea and is being evaluated for tardive dyskinesia (TD).

OBJECTIVE: To assess the effect of deutetrabenazine on cardiac repolarization.

METHODS: A QT interval study was performed to evaluate effects of deutetrabenazine 12 and 24 mg on cardiac repolarization, as assessed by time-matched change from baseline, placebo-adjusted, in Fridericia-corrected QT interval (ΔΔQTcF). Moxifloxacin (400 mg) and tetrabenazine (50 mg) were the positive control and comparator, respectively. An exposure–response analysis was developed from this study to predict maximal effects on QTcF at maximum recommended dosing based on CYP2D6 status, an approach consistent with regulatory guidance at predicting QT interval effects.

RESULTS: Maximal ΔΔQTcF between the least-squares mean (90% two-sided confidence interval) of deutetrabenazine 12 and 24 mg (n = 45 in each group) were 2.8 (0.7–4.8) ms and 4.5 (2.4–6.5) ms, respectively. The ΔΔQTcF increase with tetrabenazine (n = 45) was 7.6 (5.6–9.5) ms. Assay sensitivity was verified with moxifloxacin (n = 47), which produced a maximal effect on ΔΔQTcF of 14.0 (11.9–16.0) ms. A linear model was developed that described a correlation between plasma concentrations from pivotal HD andTD trials (n = 101) and QT interval prolongation. Using that model and the individual predicted Cmax for HD and TD patients, the placebo-adjusted change from baseline inQTcF for deutetrabenazine at maximal recommended daily doses was found to be 5.4 (2.5–9.5) ms.

CONCLUSIONS: Patients receiving the maximal recommended doses of deutetrabenazine are predicted to have a QTcF increase below the level of regulatory concern.

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Effect of DR/ER-MPH on Early Morning and Late Afternoon/Evening Functioning in Children With ADHD: Analysis of PREMB-R Items From a Phase 3 Trial

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ABSTRACT: Objective: In a phase 3 trial of children with ADHD, DR/ER-MPH (formerly HLD200), a delayed-release and extended-release methylphenidate, improved ADHD symptoms and reduced at-home early morning and late afternoon/evening functional impairments versus placebo, as measured by the validated Parent Rating of Evening andMorning Behaviors-Revised, Morning (PREMB-R AM) and Evening (PREMB-R PM) subscales. This post hoc analysis evaluated the effect of DR/ER-MPH versus placebo onindividual PREMB-R AM/PM item scores.

METHOD: Data were analyzed from a pivotal, randomized, double-blind, multicenter, placebo-controlled, parallel-group, phase 3 trial of DR/ER-MPH in children (6-12 years) withADHD (NCT02520388). Using the 3-item PREMB-R AM and 8-item PREMB-R PM, both key secondary endpoints, investigators evaluated early morning and lateafternoon/evening functional impairment by scoring each item on a severity scale from 0 (none) to 3 (a lot). For post hoc analyses, treatment comparisons between DR/ER-MPH and placebo at endpoint were determined by using least squares mean changes from

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