12 per Clinical Global Impression of Change (GIC); 23 or 49 (47%) per Patient GIC. Total motor AIMS scores were reduced by 4.8 points at week 12. Among the 39 (78%) patients who responded to the questionnaire, 72% found it easy to understand when/which dosage to take, 77% easy to remember to take their medication, 74% easy to change the dose weekly, 69% easy to follow kit instructions, and 77% easy to use the kit overall.

Conclusions. 78% of patients with TD successfully completed the 4-week titration kit in approximately 4 weeks, with adherence rates of 97.2%. 95% of patients reaching week 12 had a maintenance dosage ≥24 mg/day. 49% of patients achieved treatment success based on Clinical GIC. Patients reported high levels of satisfaction with the titration kit and 77% found it easy to use. The 4-week patient titration kit enabled patients to titrate DTBZ to an optimal dosage and experience effectiveness similar to the pivotal clinical trials.

Funding. Teva Branded Pharmaceutical Products R&D, Inc.

Evaluating Viloxazine ER (Qelbree) Administered with Psychostimulants For Pediatric ADHD: Analysis of a Phase 4 Safety Trial

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Introduction. Viloxazine extended-release (ER) is an FDA-approved, nonstimulant medication for pediatric (≥6 years) and adult ADHD. Apart from use as monotherapy, nonstimulants may be combined with stimulants when patients experience inadequate response or difficulties with medication tolerability. This phase IV, open-label trial (NCT04786990) evaluated the safety and tolerability of viloxazine ER administration with psychostimulants in children and adolescents with ADHD. Differences between morning and evening use of viloxazine ER were also assessed.

Methods. Children and adolescents (6 – 17 years) experiencing inadequate response (ADHDRS-5 ≥24 and CGI-S ≥3) to psychostimulant treatment (methylphenidate or amphetamine) were enrolled. Subjects maintained stable stimulant use throughout the trial. Following an up to 4-week screening period, subjects continuing to show inadequate response received flexibly dosed viloxazine ER (100-400 mg/day children; 200-600 mg/day adolescents) each morning during Weeks 1-4 and each evening during Weeks 5-8. Safety, tolerability, and efficacy were assessed relative to Baseline, and for change from baseline for morning vs. evening dosing.

Results. 56 subjects received viloxazine ER with 85.7% of these completing the study. Adverse events were reported by 55.4% of subjects, most commonly headache (17.9%), decreased appetite (12.5%), and upper respiratory tract infection (10.7%); onset was more common during AM dosing trial weeks [50% of subjects reported AEs during Weeks 1-4 and 36% during Weeks 5-8]. AEs were largely mild (32.1%) or moderate (21.4%) and led to discontinuation for 2 (3.6%) subjects. Baseline mean (SD) Investigator Rated-ADHD-Rating Scale 5th ed. (IR-ADHD-RS-5) score was 37.2 (8.35), n=56. Significant improvement in IR-ADHD-RS-5 was seen by Week 1[-6.9 (8.16), n=56; P<.0001)] and continued through Weeks 4 and 8 [-13.5 (9.70) p<.0001 and -18.2 (9.99) p<.0001, respectively]. Over 50% of subjects were rated much or very much improved on CGI-I at endpoint. Scores on the sleep disturbance Scale for Children (SDSC) scale also improved at both Weeks 4 and 8 [-8.8 (14.03) P<.0001 and -10.3(17.39) P=.0002, respectively], as did Parent-ratings of morning and evening ADHD symptoms and behavior, suggesting that morning and evening administration of viloxazine ER were both efficacious.

Conclusions. Viloxazine ER showed acceptable safety and tolerability when administered with stimulant medications in this Phase IV open-label trial. Administration of viloxazine ER in the evening instead of the morning did not appear to affect safety, nor the trajectory of drug response or sleep improvement.

Funding. Supernus Pharmaceuticals, Inc.

Qelbree (viloxazine extended-release capsules): Final Results of the Long-Term, Phase 3, Open-Label Extension Trial in Adults with ADHD

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Introduction. Viloxazine extended-release (ER) is an FDA-approved nonstimulant medication for ADHD in children (≥6 years) and adults. Approval in adults was based on a double-blind (DB) pivotal trial [NCT04016779] showing statistically significant efficacy on the Adult ADHD Investigator Symptom Rating Scale (AISRS; primary outcome). Here we report final results from the long-term, open-label extension (OLE) safety trial [NCT04143217] conducted as a following to the DB trial.

Methods. Upon completing DB treatment, consenting subjects who enrolled in the OLE received viloxazine ER 200 mg/day, with flexible titration to an optimal maintenance dose (200-600 mg/day). Addition of a stimulant was permitted, at investigator's discretion, following Week 12. OLE trial enrollment was

https://doi.org/10.1017/S1092852924001263 Published online by Cambridge University Press

temporarily closed at the outset of the COVID pandemic. Subjects completing the DB during this time were allowed delayed entry into the OLE upon requalification. Safety and efficacy measures were assessed relative to DB (or OLE re-entry) Baseline) at OLE Weeks 2, 4, and ~ every 8 weeks thereafter. The trial was planned for 3 years or until commercial availability of viloxazine ER.

Results. Subjects (N= 159; including 133 immediate- and 26 delayed-rollover) received viloxazine ER for 265 ± 254.9 days (mean ± SD). Nine subjects used adjunctive stimulant medication at some point after Week 12. Primary reasons for discontinuation included withdrawal of consent (25.6%), loss to follow up (17.7%), and adverse events (17.6%). Adverse events (experienced by 72.3%) were largely mild (26.4%) or moderate (40.3%) in severity and included (≥10%) insomnia (13.8%), nausea (13.8%), headache (10.7%), and fatigue (10.1%). Changes in clinical laboratory measures, vital signs, and ECG parameters were consistent with those observed in DB and product labeling. Suicidal ideation (wish to be dead) was reported by 3 subjects at a single visit each; no subject reported suicidal behavior. ADHD symptom (AISRS), executive function (BRIEF-A), global function (CGI), and quality of life (AAQOL) measures showed continued improvement in the OLE relative to that seen in DB. Baseline [mean ± SD)] AISRS Total, CGI-S, BRIEF-A GEC T-score and AAQOL ratings, respectively, were 37.9 ± 6.34), 4.6 ± 0.60, 70.4 ± 10.94 and 54.9 ± 14.96. All showed significant improvement (P<.0001 relative to Baseline) by the first OLE follow-up assessment (Week 2 for AISRS and CGI-S, Week 4 for BRIEF-A and AAQOL). Improvement continued with long-term use. Subjects maintained on viloxazine ER for at least 3 months (≥ Week 12) showed changes at Last OLE Visit of -20.0 ± 11.63 (n=106), -1.8 ± 1.34, -13.6 ± 13.64 (n=104), and 12.7 ± 17.90 (n=87) respectively.

Conclusions. Subjects maintained on viloxazine ER showed continued improvement in ADHD symptoms, global and executive function, and quality of life measures during long-term treatment.

Funding. Supernus Pharmaceuticals, Inc.

Cogwheel Rigidity in Subacute Combined Degeneration Unresponsive to Vitamin B12 Therapy

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Introduction. Parkinsonian symptoms seen with B12 deficiency have been described in five cases where B12 therapy has led to their elimination. Subacute combined degeneration (SCD) presenting with parkinsonian signs of cogwheel rigidity, unresponsive to B12 supplementation, has not heretofore been described.

Methods. Case Study: This 62-year-old right-handed woman with a past medical history of hypothyroidism presented with complaints of trouble with memory. Cogwheel rigidity and pernicious anemia with low intrinsic factor and B12 levels (165 pg/ml) were found. SCD was diagnosed and treated with monthly B12 injections over the past three years, providing symptomatic relief, yet the cogwheeling persisted. She described never developing trouble with gait, movement disorders, autonomic abnormalities, olfactory dysfunction, disorders of sleep, visual hallucinations, or other parkinsonian symptoms.

Results. Abnormalities in Neurologic Examination: Cranial Nerve (CN) Examination: CN I: Alcohol Sniff Test: 9 (hyposmia). CN III, IV, VI: Bilateral ptosis. Motor Examination: 1+ Cogwheel rigidity both upper extremities. Drift Testing: Right pronator drift with left abductor digiti minimi sign. Reflexes: 3+ throughout other than 4+ ankle jerks. Quadriceps femoris bilaterally pendular. Bilateral Hoffman and Babinski reflexes present. B12 Level: 394 pg/ml (normal).

Discussion. While predominantly affecting the posterior columns and the lateral corticospinal tract, the demyelination may further extend into adjacent fibers including the reticulospinal tract and the rubrospinal tract, the tracts which, in Parkinson's Disease, have been cited for their role in maintenance of tone and thus cogwheeling. Additionally, low B12 and elevated homocysteine levels have been noted as potential contributory factors in the pathogenesis of Parkinson's Disease. It is also possible that this is a violation of Occam's razor, that this individual has two separate distinct diseases — the prominent subacute combined degeneration as well as a subclinical parkinsonism which was revealed on neurologic examination. The parkinsonian signs may have been present prior to the B12 deficiency, and if not for the examination findings, could have remained undiscovered for decades. In those that present with Subacute Combined Degeneration, evaluation for parkinsonism is warranted.

Funding. No Funding

Pseudo-Wellens Syndrome: Demonstrating the Importance of Electrocardiogram in Emergency Psychiatric Patients

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Introduction. Pseudo-Wellens syndrome (PWS) is a rare but clinically significant condition characterized by electrocardiogram (ECG) abnormalities that mimic acute ST-segment elevation myocardial infarction (STEMI) in the absence of obstructive lesions on coronary angiography. The occurrence of PWS should be on the differential for any patient who visits the Emergency Room

https://doi.org/10.1017/S1092852924001263 Published online by Cambridge University Press