

T-032

A population PKPD Model for Changes in Sexual Function Questionnaire (CSFQ) in Patients with Major Depressive Disorder (MDD) Treated with Vilazodone or Placebo

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Objectives: Characterize the relationship between vilazodone plasma exposures (AUC) and changes in sexual function.

Methods: A PKPD model using a nonlinear mixed-effect modeling approach was used to explore the relationship between plasma levels of vilazodone (described by AUC) and longitudinal Changes in Sexual Functioning Questionnaire (CSFQ scores). Data from a double-blind, placebo and active-controlled Phase 4 clinical study in patients with MDD were used for these analyses. The data included placebo and two vilazodone treatment arms (20 and 40 mg/day). A previously developed population PK model for vilazodone was used to predict AUC for each patient. Linear and Emax exposure-response relationships were investigated. In addition to drug effect, placebo effect and covariate-parameter relationships were explored. Montgomery-Åsberg Depression Rating Scale total scores (MADRS), were included in the PK-CSFQ model as a covariate.

Results: Exploratory graphical analysis indicated that changes in CSFQ were correlated with changes in MADRS across placebo and active treatment arms. There was no evidence of relationship between CSFQ and vilazodone exposures. During model development, CSFQ scores were primarily thought to be influenced by two factors: 1) MADRS (improvement or worsening of depression might have an impact on patient's sexual function), and 2) vilazodone exposures. Final exposure-response model for CSFQ identified the time-varying MADRS score to be a statistically significant predictor of the placebo response (worse MADRS depression symptoms were associated with worse CSFQ). After controlling for MADRS, no additional statistically significant effect of vilazodone on CSFQ over time could be detected ($p > 0.05$).

Conclusions: After accounting for MADRS total score, no additional effect of vilazodone exposures on sexual function (as measured by CSFQ total score) over time could be detected. Thus, vilazodone can be expected to improve sexual function in MDD patients by reducing depressive symptoms, while, it does not have any additional direct effect on sexual function.