

Title: DEVELOPING CLINICALLY MEANINGFUL RESPONDER THRESHOLDS FOR PRIMARY ENDPOINTS FOR CLINICAL TRIALS IN PREMENOPAUSAL WOMEN WITH HYPOACTIVE SEXUAL DESIRE DISORDER

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The Methodological Question Being Addressed: Do Female Sexual Function Inventory Desire scale (FSFI-D) and the Female Sexual Distress Scale-revised question 13 (FSDS-R Q13) scores support the validity of responder definitions for women receiving bremelanotide for the treatment of hypoactive sexual desire disorder (HSDD)?

Introduction (Aims):

Clinically meaningful responder definitions are needed to assist clinicians and regulatory agencies in evaluating the clinical significance of treatment differences. For clinical trials evaluating primary and secondary endpoints based on patient-reported outcomes, including those for HSDD, these interpretation guidelines for clinically meaningful responses are essential. The objective of this study was to identify and support the validity of responder definitions for the FSFI-D and the FSDS-DAO Q13 scores. Anchor-based methods were used to determine clinically meaningful responder thresholds.

Methods:

An independent anchor assessment committee (IAAC) was established to conduct a blinded, psychometric analysis of data collected from two Phase 3 BMT studies (RECONNECT) in 1202 women with HSDD. One dynamic anchor (treatment benefit scale), and three static anchors (desire/interest with sexual activity; satisfaction with sex life; distress about sex life) were selected for this analysis. Mean and median baseline to endpoint changes in FSFI-D and FSDS-DAO Q13 scores were examined by responder definitions based on these four anchors. Results were reviewed by the IAAC and recommendations were made on responder thresholds for the FSFI-D and FSDS-DAO Q13 scores. Post-study exit survey (n=243) data were used to further support the validity of the responder thresholds by evaluating the relationship between overall treatment benefit versus changes in FSFI-D and FSDS-DAO Q13 scores.

Results:

For the treatment benefit dynamic anchor for the FSFI-D, median and mean change scores were 0.6 and 0.85, respectively. The median and mean change scores for the treatment benefit dynamic anchor for the FSDS-DAO Q13 were 1.0 and 0.9, respectively. Based on the pooled psychometric analyses, the anchor-based results supported as clinically meaningful, a 0.6 point change in FSFI-D scores (range 0.6–1.2), and a 1.0 change in FSDS-DAO Q13 scores (range 0.9-

1.0). The exit survey question on overall treatment benefit demonstrated a percentage agreement of 89% and kappa of 0.77 with the anchor threshold of  $\geq 5$  on the dynamic anchor, representing a response of better or much better, indicating excellent agreement. The recommended responder thresholds for the FSFI-D and FSDS-R were supported by the exit survey treatment benefit question.

#### Conclusions:

Based on the psychometric analyses, a change of  $\geq 0.6$  points in FSFI-D and  $>1.0$  points in FSDS-DAO question 13 were recommended for defining clinical significance of treatment benefits of BMT.

#### Disclosures:

Revicki is a consultant, advisory board member or investigator for Palatin Technologies; AMAG.

Clayton is a consultant, advisory board member or investigator for Axsome; Endoceutics; Fabre-Kramer; Forest Research Institute, Inc., now Allergan; Janssen; Palatin Technologies; S1 Biopharma; Sage; Sprout, a division of Valeant Pharmaceuticals; Takeda. Clayton has Shares/Restricted Stock Units: Euthymics; S1 Biopharma; and Royalties/Copyright: Ballantine Books/ Random House; Changes in Sexual Functioning Questionnaire; Guilford Publications.

Stouch is a consultant for Palatin Technologies.

Portman is a consultant, speaker's bureau; or investigator for Palatin Technologies; Endoceutics; AMAG; Sprout. Portman is an employee and shareholder: Sermonix Pharmaceuticals

Kingsberg is a consultant, advisory board member or investigator for AMAG, Endoceutics, TherapeuticsMD, Pfizer, Palatin Technologies, Emotional Brain, Valeant Pharmaceuticals, Sermonix Pharmaceuticals, Duchesney, Acerus, Materna, Strategic Scientific Solutions (SST), Lupin.

Derogatis is a consultant and investigator for Palatin technologies.

Robert Jordan is an employee and has stock in Palatin Technologies.