No food effect was observed for AMPH ER TAB administered chewed. All AEs were mild in severity and AE profiles were similar to other amphetamine formulations used for treatment of ADHD.
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Palatability Assessment of a New Amphetamine Extended-Release Tablet Formulation

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ABSTRACT: Background: In 2016, the US FDA issued an industry guidance document "Quality Attribute Considerations for Chewable Tablets" which describes the quality attributes to be considered when developing chewable tablets. It includes recommendations on selection of acceptance criteria for measuring palatability (having a taste acceptable to the patient or has adequate masking). These data are now recommended as part of ANDA submissions. Palatability is a known positive contributing factor to drug adherence and persistence. We summarize here palatability data for a new amphetamine extended-release tablet (Dyanavel XR® Extended Release Tablet; AMPH ER TAB).

METHODS: This was a 2-arm preplanned secondary analysis from a comparative bioavailability study: single-dose AMPH ER TAB 20 mg chewed under fasting (Treatment A) and fed (Treatment B) conditions. Subjects rated the palatability of AMPH ER TAB (Treatments A+B) through a 5-question palatability questionnaire. The questions included in the palatability questionnaire were as follows:

1. Oral sensation/mouth feel of the drug product
2. Taste of the drug product
3. How strong is the taste?
4. Aftertaste of the product
5. How strong is the aftertaste?

Subjects completed the questionnaire within 10 minutes from the time of drug administration, which was evaluated and scored according to the rubric below:
Q1, Q2, Q4: palatability- Very unpleasant (score of 1), Unpleasant (2), No sensation or mouthfeel (3), Pleasant (4), and Very pleasant (5)
Q3, Q5 (Taste/aftertaste strength): Very strong (score of 1), Strong (2), Moderate (3), Mild (4), No aftertaste (5).
Scores of 1-2 for both categories were Negative; score of 3 was Neutral, and 4-5 were Positive.

RESULTS: 35 subjects comprised the palatability dataset (completed one question on the questionnaire). In the palatability analysis, for treatments A and B, most of the subjects rated the oral sensation/mouth feel of AMPH ER TAB (Question 1) and the taste of AMPH ER TAB (Question 2) as positive (pleasant to very pleasant) (70.1% and 83.6%, respectively). When evaluating taste strength (Question 3): 43.3% rated the strength as positive (mild/no taste) and 43.3% of subjects rated the strength as neutral (moderate taste). Also, 82.1% rated the aftertaste of AMPH ER TAB (Question 4) as positive (pleasant/very pleasant) and 52.2% rated the strength of the aftertaste as positive (mild/no taste).

CONCLUSION: Most subjects rated the oral sensation and taste as pleasant or very pleasant, whether chewed under fasted conditions or after a meal. With respect to the taste strength, most subjects rated it as moderate (chewed under fasted conditions) or mild/no taste (chewed after a meal). Aftertaste was rated as pleasant or very pleasant in most subjects, with the strength as moderate (chewed under fasted conditions) or mild/no aftertaste (chewed after a meal). AMPH ER Tablets provided an overall pleasant taste and mouthfeel experience for patients.
Funding Acknowledgements: Tris Pharma, Inc.

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Improvement of Sexual Function Observed During Treatment of Major Depressive Disorder with Adjunctive Pimavanserin

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ABSTRACT: Study Objectives: Sexual dysfunction occurs in 40%-60% of patients with major depressive disorder (MDD), due to either the illness itself and/or the effects of antidepressant treatment. The phase-2 CLARITY trial recently demonstrated the efficacy of adjunctive pimavanserin (PIM) for MDD when added to ongoing selective serotonin or serotonin–norepinephrine reuptake inhibitor (SSRI/SNRI) treatment. No new safety observations were reported in this study. This post-hoc analysis examines the potential impact of PIM treatment on sexual function.

METHOD: Study methodology has been presented previously (APA 2019). Adult male and female patients with moderate-to-severe MDD were randomized to PIM 34 mg/day (n=51) or placebo (PBO, n=152) added to ongoing SSRI/SNRI treatment. Massachusetts General Hospital–Sexual Functioning Inventory (MGH-SFI) and Hamilton Depression Rating Scale, 17-item version (HAMD-17) item 14 (sexual interest) scores were examined by analysis of covariance.

RESULTS: Adjunctive PIM resulted in significantly greater 5-week reduction (improvement) relative to SSRI/SNRI treatment plus placebo on mean MGH-SFI scores (difference –0.634, SE 0.167; P<0.001; effect size [ES], Cohen's d 0.614). Similarly, PIM resulted in greater improvement compared with placebo on individual MGH-SFI items that applied to both males and females: Interest in Sex (P=0.006; ES=0.483), Ability to Get Sexually Aroused/Excited (P=0.001; ES=0.560), Ability to Achieve Orgasm (P<0.001; ES=0.609), Overall Sexual Satisfaction (P=0.003; ES=0.524). HAMD-17 item 14 scores were also significantly more reduced (improved) with PIM (P<0.001; ES=0.574).

CONCLUSIONS: These results underscore the potential of adjunctive PIM for improving sexual function in patients with MDD and inadequate response to SSRIs/SNRIs. Potential benefits should be confirmed in further studies. Funding Acknowledgements: ACADIA Pharmaceuticals Inc.

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A Phase-2 Sequential Parallel Comparison Design Study to Evaluate the Efficacy and Safety of Adjunctive Pimavanserin in Major Depressive Disorder

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ABSTRACT: Study Objectives: Depression is the leading cause of disability worldwide, with fewer than 50% of treated patients achieving full remission. This study ("CLARITY," ACP-103-042: NCT03018340) examined the 5-HT2A inverse agonist pimavanserin (PIM) as a potential adjunctive treatment for major depressive disorder (MDD).

METHOD: Adult female and male subjects with a DSM-5 primary diagnosis of a major depressive episode as part of MDD, inadequate response to ongoing SSRIs or SNRIs of adequate dose and duration as confirmed by the Massachusetts General Hospital Antidepressant Treatment History Questionnaire, and a MADRS total score >20 were randomized to PIM 34 mg/day or placebo (PBO) added to their SSRI/SNRI treatment. A sequential parallel comparison design was used, consisting of two 5-week stages. PBO nonresponders in Stage-1 who met prespecified criteria were re-randomized to PIM or PBO for the second period (Stage-2). The primary efficacy measure was the weighted average of Stage-1 and Stage-2 total scores of the HAMD-17.

RESULTS: Of the 207 patients enrolled, 52 received PIM, and 155 received PBO in Stage 1. Mean age was 46.2 years, and 72.9% of patients were female. Baseline MADRS total (mean [SD]: 31.5 [0.4]) and HAMD-17 total scores (22.2 [0.3]) indicated a moderate overall severity of illness. PIM met the primary endpoint, reducing the weighted Stage-1/Stage-2 HAMD-17 total score relative to PBO (least-square means [LSM] difference, –1.7; standard error [SE], 0.9; P=0.04). Stage-1 PIM patients demonstrated highly significant 5-week improvement on the HAMD-17 (LSM difference=–4.0, SE=1.1; P<0.001; effect size, Cohen's d: 0.626), separating from placebo by the end of Week 1 (LSM difference=–1.7, SE=0.8; P=0.04). Stage-2 results showed no significant separation among Stage-1 placebo nonresponders (P=0.69). In Stage 2, a substantively smaller

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