Conclusion: In OSA patients with a moderately collapsible upper airway, the combination of atomoxetine plus trazodone yielded clinically meaningful improvements in measures of sleep disordered breathing and oxygenation while atomoxetine plus lemborexant produced smaller effects.
Support (If Any): This study was supported by Apnimed.

0755

COMPARISON OF CLINICAL PATHWAYS FOR UPPER AIRWAY STIMULATION MANAGEMENT: IN-LABORATORY TITRATION POLYSOMNOGRAPHY VERSUS HOME-BASED EFFICACY SLEEP TESTING

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Introduction: Upper airway stimulation (UAS) therapy is an alternative treatment option for select CPAP-intolerant patients with obstructive sleep apnea. Current standard-of-care management uses in-laboratory polysomnography for titration of UAS stimulation amplitude (tPSG) after 3 months of patient self-titration at home. This home monitoring study was designed to evaluate whether tPSG or efficacy home sleep test (eHST) with tPSG by exception for eHST non-responders would have non-inferior apnea-hypopnea index (AHI) outcomes.
Methods: Enrolled patients underwent UAS implantation as part of regular clinical care and were randomized at the activation visit 1:1 between tPSG or eHST for the 3-month post-activation visit. If eHST results were suboptimal (AHI > 15 events/h or < 50% reduction from baseline AHI) patients underwent tPSG titration at 5 months. Both groups had 2-night eHSTs at 6 months post-activation. The primary endpoint was 6-month AHI equivalence between arms (defined as ± 15 events/h). Secondary endpoints were equivalence of Epworth Sleepiness Score (ESS; ± 2), oxygen desaturation index (ODI; ± 15 events/h), and nightly UAS device usage (± 0.5 h).
Results: The study randomized 60 patients from August 2020 through September 2021, who were primarily middle aged (57 ± 10 years), male (67%), Caucasian (98%), and overweight (BMI 29 ± 3 kg/m2), with severe OSA (AHI 35 ± 16). Eleven patients withdrew from the study early. As of December 2021, 41 and 36 patients have completed 3- and 6-month follow-up visits, respectively. Six-month visit AHI, ESS, ODI, and device usage data between arms is currently blinded and is expected to be complete by Q2 2021 prior to SLEEP 2022.
Conclusion: If the study demonstrates equivalent 6-month AHI, ESS, ODI, and usage outcomes, the use of eHST to ascertain therapy efficacy prior to tPSG could be a non-inferior alternative management option to tPSG.
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0756

PRECLINICAL PHARMACOLOGY OF SOLRIAMFETOL: POTENTIAL MECHANISMS FOR WAKE PROMOTION

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Introduction: Solriamfetol is a wake-promoting agent (WPA) approved for the treatment of excessive daytime sleepiness associated with narcolepsy and obstructive sleep apnea. The wake-promoting mechanism of solriamfetol may result from dopamine and norepinephrine reuptake inhibition. Preclinical pharmacology studies were conducted to further elucidate the molecular targets activated by solriamfetol and compare them to that of known WPAs and traditional stimulants.
Methods: In vitro binding and functional studies were conducted in a panel of cell lines or membrane preparations expressing transmembrane receptors and monoamine transporters to measure the activity of solriamfetol, comparator WPAs, and traditional stimulants. Electrophysiology studies were conducted in slice preparations from mouse ventral tegmental area (VTA). Studies to measure locomotor activity and wake-promoting effects were conducted in mice.
Results: In vitro functional studies showed agonist activity of solriamfetol at human, mouse, and rat TAAR1 receptors. hTAAR1 EC50 values (10–16 µM) were within the clinically observed therapeutic solriamfetol plasma concentration range and overlapped with the observed DAT/NET inhibitory potencies of solriamfetol in vitro. TAAR1 agonist activity was unique to solriamfetol; neither the WPA modafinil nor the DAT/NET inhibitor bupropion had TAAR1 agonist activity. Solriamfetol (1–10 µM) dose-dependently inhibited the firing frequency of dopaminergic VTA neurons in mouse brain slices, similar to known TAAR1 agonists; however, these effects were inhibited by a D2 antagonist, suggesting a DAT-mediated effect. Unlike traditional stimulants, solriamfetol did not increase locomotor activity in naive mice, but inhibited the increase in locomotor activity in DAT knockout mice.
Conclusion: Preclinical studies have identified agonist activity at the TAAR1 receptor and, possibly, lower potency agonist activity at 5-HT1A receptors as potential pharmacological targets for solriamfetol, in addition to its activity as a DAT/NET inhibitor. Given the current understanding of TAAR1 agonists as modulators of monoamine transmission with potential wake-promoting effects in multiple preclinical species, agonist activity at the hTAAR1 receptor may represent an additional pharmacological target underlying the wake-promoting effects for solriamfetol, in addition to its DNRI activity.
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0757

CLUSTER ANALYSIS FOR IDENTIFYING GOOD CPAP ADHERENCE USING THE PSG PARAMETERS AND PATIENT CHARACTERISTICS

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Introduction: CPAP is the standard treatment for obstructive sleep apnea (OSA). One of the important clinical issues to be solved is poor CPAP adherence. A growing body of studies has identified predictive factors for CPAP adherence including AHI, BMI, age, gender, symptoms, etc. When our sleep physicians prescribe CPAP, we would consider these known factors in multiple ways. One may want to know factors' combinations rather than each factor. In this case, cluster analysis might be useful since it is a