are not statistically significant, and/or show an advantage for PIM over placebo (such as for postural hypotension), denoting that PIM is a potentially tolerable intervention. In terms of LHH, PIM 34 mg/d is about 5 times more likely to result in clinical response (as measured by ≥3 point decrease from baseline on the SAPS-PD) vs. discontinuation due to an adverse event.

CONCLUSIONS: Using the metrics of NNT, NNH, and LHH, PIM 34 mg/d for the treatment of PDP appears to have a compelling benefit-risk profile.

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155 Improvement of VIIIth Cranial Nerve Function With Cariprazine

Maximus K. Philobos, MS4; and Alan R. Hirsch, MD2
1 Avalon University School of Medicine, Willemstad, Curacao
2 Smell and Taste Treatment and Research Foundation, Chicago, IL

ABSTRACT: Introduction: Cariprazine an atypical antipsychotic which acts as a dopamine D3-prefering partial agonist at dopamine D2/D3 receptors, as an antagonist at over stimulated dopamine receptors, as a partial agonist at serotonin 5-HT1A receptors, and as an antagonist of 5-HT2A receptors (Citrome, 2016; Kiss, 2010). While indicated for the treatment of schizophrenia and bipolar disorder, it has never been described to improve disorders of cranial nerve VIII. A patient with hearing loss associated with tinnitus, responsive to cariprazine, is reported.

METHODS: Case Study: A 34 year old right handed married male 5 years prior to presentation developed bilateral auditory hallucinations of whispers, and one male disparaging voice. Approximately 6 months later it began belittling him, whereupon he was diagnosed with schizoaffective disorder, attention deficit hyperactivity disorder, and obsessive-compulsive disorder. Three months prior to presentation he developed sepsis and became comatose. Upon awakening he experienced constant tinnitus, AS more than AD high pitched, without diurnal variation, which has been unrelenting. Coincident with the tinnitus was decreased hearing AS more than AD. Within a few days of treatment with cariprazine at 1.5 mg a day, the tinnitus transiently resolved and after raising the cariprazine to 3 mg per day the tinnitus abruptly stopped and his hearing returned to normal after 2 months. One and a half days after discontinuing the cariprazine the tinnitus and hearing loss returned. After reinstating the cariprazine to 3 mg a day the tinnitus and hearing loss resolved again.


DISCUSSION: In the cochlea, as an inhibitory neurotransmitter, dopamine reduces sensitivity to auditory sensation (Langguth, 2009). Since ambient sounds are known to reduce tinnitus (masking), an antagonist at over-stimulated dopamine receptors, cariprazine may act to reduce dopamine’s effectiveness, reducing inhibition and thus enhancing perceived external sound. It may act as a 5-HT1A serotonin agonist, directly reducing tinnitus. With reduced tinnitus there is less of a distraction and thus enhanced hearing. Or its function may be through its neuroleptic effects; the tinnitus could be a manifestation of auditory hallucinations, through reduction of this noise cariprazine secondarily causes enhanced hearing. Further investigation into the use of cariprazine in those with intractable tinnitus is worthwhile.

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156 Improvement in Disease Severity in Patients With Treatment-Resistant Depression Following Treatment With Intranasal Esketamine

Abigail Nash, MD, PhD1; May Shawi, PhD2; Jaskaran Singh, MD3; Ella Daly, MD4; Kimberly Copper, MS5; Pilar Lim, PhD4; Rosanne Lane, MAS3; Jagadish Gogate, PhD4; Allitia DiBernardo, MD4; David Hough, MD4; and Larry Alphs, MD, PhD2
1 Janssen Global Services, New Jersey
2 Janssen Scientific Affairs, New Jersey
3 Janssen R&D, California
4 Janssen R&D, New Jersey

ABSTRACT: Background: Recognizing the importance not only of the clinician’s opinion but also of the patient’s experience and perspective, Sequenced Treatment Alternatives to Relieve Depression (STAR*D) utilized both clinician-reported and patient-reported outcomes in a large-scale multi-step study on antidepressant effectiveness in real-world settings. Both approaches indicate
that <17% of Major Depressive Disorder (MDD) patients respond to novel oral treatments after two prior antidepressant failures. To address this low response rate and continue to investigate the use of patient-rated outcomes in clinical trials, an antidepressant with a new mechanism of action is being investigated for efficacy and safety utilizing both clinician-rated and patient-reported scales.

**METHODS:** This is a post-hoc analysis of a Janssen R&D Phase 2a clinical trial (ESKETINTRD2005). Subjects aged 20-64 with MDD without psychotic features (DSM IV) and a history of inadequate response to ≥2 antidepressants were randomized [3:1:1:1] to 1 week of twice-weekly treatment with intranasal placebo (n = 33), esketamine 28 mg (n = 11), 56 mg (n = 11), or 84 mg (n = 12). Participants taking oral antidepressants at study entry continued treatment during the study. Changes in depression severity were measured using the Clinical Global Impression Severity (CGI-S) and the Patient Global Impression Severity (PGI-S) scales.

**RESULTS:** At all esketamine doses (28 mg, 56 mg, 84 mg), subjects reported a one-point mean change in CGI-S from baseline to week one compared to no change on placebo (p-values 0.005, 0.001, 0.032 respectively). Similarly, mean CGI-S scores improved for subjects receiving esketamine at all doses (p-values 0.028, 0.004, 0.049 respectively) compared to no change in placebo subjects. These data are consistent with previously reported data based on the Montgomery Åsberg Depression Rating Scale (MADRS) and support positive correlation between patient-reported and clinician-reported outcomes.

**DISCUSSION:** Initial results from this Phase 2a study suggest clinically relevant improvement in depression symptoms in as early as one week when treated with twice-weekly intranasal esketamine as reported by both clinicians and patients. This work will help guide future investigations of esketamine in larger populations to provide better therapeutic options for treatment-resistant MDD patients.

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**ABSTRACT:** We present a case of a 66 year old Caucasian female with Bipolar type 1 disorder, status post right renal transplant (5/8/14) on maintenance immunosuppression who presented with mania and psychosis. The previous weeks had her being sleep deprived, talkative, making random calls to family members at odd hours, demonstrating pressured speech and also having erotomania regarding Joshua Bell, the violinist. She had recently been switched from Divalproex sodium (on which she had been stable for years) to Quetiapine due to thrombocytopenia attributed to the former. Quetiapine was optimized to 800 mg over two weeks without any improvement. She continued to be severely manic with new delusions of being in a World War II zone and the staff being NAZIs. She continued to be tangential with disorganized behavior and inability to care for self. She was then restarted on Divalproex sodium (for mood) with close monitoring of her counts along with Risperidone (for psychosis). Divalproex sodium was optimized to 1500mg and Risperidone to 6 mg over the next 2 weeks without much improvement. Risperidone was then cross tapered with Olanzepine. We also began to pursue other causes of treatment refractory mania with psychosis, namely her immunosuppressant medications. She had been placed on maintenance immunosuppression with tacrolimus (Prograf) 3mg BID, Mycophenolic acid (Myfortic) 360 mg BID and Prednisone 5 mg. Though the most recent Tacrolimus level was within therapeutic range, they were still higher than her baseline levels. Based on few case reports of psychosis associated with Tacrolimus and per discussion with nephrology, we planned cross taper of Tacrolimus and Cyclosporin. Tacrolimus was eventually tapered off and Cyclosporine was maintained at 125 mg qam and 100 mg qpm. Prednisone was maintained at 5 mg daily. Her mania and psychosis improved and she was ultimately discharged on Olanzepine 20mg qhs, Divalproex sodium 1500mg qhs. The problems encountered during this case were plenty due to multiple comorbid conditions including a right adrenal adenoma, hypertension, impaired glucose tolerance, thyroid dysfunction, hyperlipidemia and having bio-prosthetic aortic valve due to Aortic stenosis (2013). In conclusion, psychosis can be precipitated in renal transplant patient with Bipolar disorder I with previously maintained stability on Tacrolimus with other comorbid conditions. So, It would be important to re-evaluate the use of Tacrolimus or the possibility of switching to another immunosuppressive agent with careful consideration of risks versus benefits. Case