related to antipsychotic treatment. However the absence of rise in oxidative stress in the group who were treated with ECT+AP suggests that, ECT+AP treatment neither constitute an additional burden nor has a positive effect on oxidative stress.

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P.2.d.019 Asenapine in the treatment of bipolar 1 disorder: a 12 months study

A. Fernandez Galvez[1], S.L. Romero Guillena[1]*, M.E. Dominguez Ballesteros[1] *[1]Unidad de gestion clinica de salud mental área hospitalaria Virgen Macarena, Mental health, Seville, Spain*

Purpose of the study: Asenapine is a multimodal action second-generation antipsychotic. In Europe, asenapine is indicates for the treatment of acute mania. The available evidence demonstrated that Asenapine is effective and generally well tolerated in the treatment of moderate to severe acute mania associated to bipolar I disorder [1–3].

The primary objective of the study was to assess long- and short-term efficacy and safety of asenapine used in common clinical practice conditions, in Type 1 bipolar patients under follow-up in a mental health community unit.

Method: Type 1 bipolar patients, who were experiencing an episode of acute mania and followed-up at the Carmona's Mental Health Community and received antipsychotic treatment with asenapine as monotherapy within a 10 to 20 mg/day dose range, were selected. The following scales were used during the 12-month follow-up period: Clinical Global Impression for Bipolar Disorder (CGI-BD-M), Young Mania Rating Scale (YMRS), Montgomery-Asberg Depression Rating Scale (MADRS), Side Effects Scale (UKU), and PRSexDQ-Salsex Sexual Dysfunction Scale. All these scales were administered at baseline, and on days 21, 90, 180, 270 and 365. The following definitions were used: Responder patient: patient who achieve a $\geqslant$50% decrease relative to the baseline value; Remitter patient: patient who achieve an YMRS score $\leqslant$12 points; Depressive episode: MADRS scale score $\geqslant$20 points. Anthropometric laboratory tests were conducted at baseline and on months 6 and 12.

Hospital admissions were collected before and after treatment initiation.

Results: A total of 20 patients on treatment with asenapine were recruited. The mean baseline YMRS scale score was 31.2 points; and the withdrawal rate was 40%. The mean change in the CGI-BD-M score at the end of the study was a reduction of 2.55 points, while a 21.7 points reduction was observed for the YMRS score. At the end of the study, the percentages of responders and remitters were 45% and 35%, respectively. The mean change in the MADRS rating scale at the end of the study was an 8.9 points increase, and no cases of depressive episode occurred.

In accordance with the UKU scale, the most common side effects were minimal to moderate severity sedation, somnolence and oral hypoesthesia, and these effects disappeared over the study period.

Sexual dysfunction was infrequent, with a prevalence of mild to moderate episodes of 25%.

Abnormalities of the metabolic profile and prolactin levels were minimal, with a mean weight decrease of 2.1 kg observed in the patient subgroup previously treated with olanzapine.

No statistically significant differences were found relative to the number of hospital admissions and mean lengths of stay.

Conclusion: Our results, obtained in a common clinical practice setting, were similar to those found in scientific literature; this allows us to conclude that asenapine shows short- and long-term efficacy for the treatment of bipolar patients.

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P.2.d.020 The effectiveness of asenapine in clinical practice: the EXPASEN study

A. Murru[1]*, N. Cruz[1], A. Gonzalez-Pinto[2], C. De Dios[3], J.M. Montes[4], A. Perez[5], I. Zorrilla[2], P. Lopez[2], E. Vieta[5] *[1]Bipolar disorders program, Department of Psychiatry, Barcelona, Spain; [2]Hospital de Alava, Department of Psychiatry, Vitoria, Spain; [3]Hospital la Paz, Department of Psychiatry, Madrid, Spain; [4]Hospital del Sureste, Department of Psychiatry, Madrid, Spain; [5]Bipolar Disorder Program, Department of Psychiatry, Barcelona, Spain*

Introduction: Asenapine is a new atypical antipsychotic that has been approved for the acute treatment of manic and mixed episodes associated with bipolar I disorder by both the FDA and the EMA, and for the treatment of schizophrenia by the FDA.

Asenapine, is a multimodal action second generation antipsychotic, with high affinity for multiple dopaminergic (D2, D3 and D4), serotonergic (5-HT_{2A}, 5-HT_{2B}, 5-HT_{2C}, 5-HT_6 and 5-HT_7) and adrenergic (α1A, α2A, α2B and α2C) receptors.

Asenapine has to be administered sublingually. Some of these actions have been linked to actions that go beyond the purely antimanic and antipsychotic antidepressant action [1].

After going through successfully the preliminary phases of development, several clinical trials have been completed in two main indications: schizophrenia and mania.

Method: EXPASEN is a retrospective study covering the clinical experience achieved on the use of asenapine in clinical practice over the past year in 4 expert Spanish centers. The anonymised records of all the patients who received asenapine in the 4 selected clinical centers were analysed. Efficacy and safety measures were collected as part of the usual care standard of the centers.

Results: Seventy-seven out of 94 patients included (82%), fulfilled criteria for bipolar disorder (BPD). Of all patients with bipolar disorder, roughly a 50% presented with an acute episode of mania, roughly a third with an acute depressive episode, 13% presented with a mixed episode and 6% were in a hypomanic episode at the time of asenapine prescription. Other diagnoses

of patients under treatment with asenapine were Schizoaffective disorder (6, 4%), Schizophrenia (6, 4%) and some eventual case of unipolar depression. Across all the above mentioned conditions, adjunctive asenapine treatment was associated to significant clinical improvements ($p < 0.001$) in all clinical scales, and was overall well tolerated. The mean daily dose used was 17 mg (N = 41) for mania, 12 mg (N = 25) for bipolar depression, 17 mg (N = 11) for mixed patients, 13 mg (N = 5) for hypomania, 18 mg (N = 5) for schizoaffective disorder (SAD), and 17 mg (N = 3) for schizophrenia (SCZ). Asenapine treatment was associated to significant improvements in several measures of effectiveness and was well tolerated. The most frequently reported adverse events were somnolence (29.8%), dysgeusia (28.7%), oral hypoaesthesia (17%), dizziness (16%), anxiety (12.8%).

Conclusions: Since its introduction, asenapine has been mostly used as adjunctive treatment in patients with bipolar disorder across several mood states. In the present study, asenapine showed efficacy not only in acute manic episodes, but also in depressive, mixed and hypomanic states and even in unipolar major depression, in schizophrenic and schizoaffective patients. Limitations include the open label design and the use of other concomitant medications. However, the EXPASEN study shows that the use of asenapine in clinical practice is consistent with the results of clinical trials [2], both from the effectiveness as well as safety perspectives, and that a number of potential new indications emerge, which should be confirmed in randomised, clinical trials.

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P.2.d.021 Lithium monotherapy versus lithium and valproate in manic and mixed states: correlation between serum lithium levels and treatment response

C. Del Grande[1], L. Musetti[1], D. Marazziti[1]*, M. Muti[2], G.U. Corsini[2], L. Dell'Osso[1] *[1]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; [2]University of Pisa, Department of Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy*

The present study aimed to evaluate the prescribing patterns of lithium, in monotherapy or in combination with valproate, in a naturalistic setting of manic and mixed bipolar patients [1]. The correlation between serum lithium levels and therapeutic response were examined in the two treatments groups, with the purpose to identify if the co-administration of the two drugs might allow to decrease serum lithium levels, while maintaining its therapeutic efficacy.

Seventy-five bipolar I patients (DSM-IV-TR), in a manic (14.7%) or mixed (85.3%) episode, treated with lithium alone (45.3%) or lithium + valproate (54.7%), were recruited and followed-up for an average period of 6±1.5 months. They were selected amongst subjects consecutively admitted at the day hospital of the psychiatric clinic of the University of Pisa, during a two-years period. Diagnosis was confirmed using the SCID-I. The CGI-BP Scale was administered, at baseline and at each subsequent check of serum lithium levels, to assess the severity of the episode. The mean sampling interval of clinical and biological evaluations was 46.5±5.7 days. The daily dose of lithium carbonate was 664±165 mg/day and that of sodium valproate 855±294 mg/day. The mean lithium level (mean±SD; mEq/L) was 0.50±0.16, while that of valproate (mean±SD; mg/L) was 54.68±23.41. The CGI-BP score for overall illness severity at baseline was 4.5±1.0.

Patients were divided in three groups according to mean lithium levels: <0.40 (n = 22, 29.3%), 0.40–0.60 (n = 33, 44%), and >0.60 (n = 20, 26.6%). The therapeutic response (reduction of the CGI-BP overall severity score between baseline and endpoint) of the patients was analyzed in relation to lithium levels and to the pharmacological treatment (lithium alone vs lithium + valproate).

The results showed that patients with lithium levels > 0.60 had higher remission rates and a greater symptom reduction than the others. Patients taking lithium plus valproate, however, showed the symptomatic improvement even with lithium levels below the therapeutic range, around 0.40. Finally, the comparison of the clinical course amongst the three groups of lithium levels in relation to the treatment with or without valproate, showed that patients of the second group (0.40–0.60) taking valproate had a higher remission rate than those with the same levels, but without valproate ($p = 0.041$). Such rate of remission was comparable to that of patients with lithium levels > 0.60, independently from the association with valproate.

These preliminary results support the efficacy of lithium for the treatment of manic/mixed episodes of moderate severity, even when administered in monotherapy, if serum lithium levels are maintained within the optimal range [2,3]. However, it can be hypothesized that valproate, at least in a subgroup of bipolar patients, might potentiate the antimanic action of lithium below the 'classical' therapeutic range, while minimizing the risk of side effects and improving tolerability of the compound.

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P.2.d.022 Cariprazine effects on YMRS items: results of a pooled analysis of 3 randomized, double-blind, placebo-controlled trials in bipolar mania

P. Keck[1], S. Zukin[2], K. Lu[2], A. Ruth[3], I. Laszlovszky[4], G. Nemeth[4], S. Durgam[2]* *[1]University of Cincinnati College of Medicine, Department of Psychiatry, Cincinnati, USA; [2]Forest Research Institute, Jersey City, USA; [3]Prescott Medical Communications Group, Chicago, USA; [4]Gedeon Richter Plc, Budapest, Hungary*

Background: Bipolar I disorder is a complex, debilitating disease with a wide specturm of symptoms that can be challenging to treat.