or antidepressants, the effectiveness of these agents remains inconsistent.

**Objective:** To present the case of a patient displaying apathy after cerebral infarction who was successfully treated for apathy with aripiprazole monotherapy.

**Case summary:** A 56-year-old woman noticed numbness in her left arm and received treatment for cerebral infarction 10 years ago. The numbness was resolved, but she continued to display severe social impairments, including a lack of initiative for housekeeping or loss of motivation for doing anything. When her husband brought her to our hospital, she was lean, disheveled, and dingy, and her verbal responses were prompt but passive. Although she was not depressed, she was assessed as having apathy because of her high score (39) on the Japanese version of Starkstein’s Apathy Scale (SAS). We initiated treatment with aripiprazole (3 mg/day) during her hospitalization. After approximately 8 weeks, her SAS score decreased to 21, and she was eventually able to participate in occupational therapy. Psychosocial and environmental support will be added to her treatment regimen because she still has some difficulty maintaining her daily routine.

**Discussion:** The pharmacological mechanism of aripiprazole for apathy treatment remains uncertain. Moreover, it is unclear whether the effectiveness of aripiprazole in this patient can be generalized to other cases of apathy.

**Conclusion:** Because aripiprazole administration was associated with partial improvement in a patient with apathy (after cerebral infarction), this agent may be considered as potential therapy for apathy.

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**PS155**

**Long-term safety of adjunctive brexpiprazole (OPC-34712) in MDD: results from two 52-week open-label studies**

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**Abstract**

**Background:** Brexpiprazole is a serotonin-dopamine activity modulator that acts as a partial agonist at 5-HT1A and dopamine D2 receptors, and an antagonist at 5-HT2A and noradrenaline alpha1B/2C receptors, all at similar potencies. The long-term safety and tolerability of adjunctive treatment with brexpiprazole were evaluated in patients with major depressive disorder and inadequate response to antidepressant treatments, based on pooled data from two open-label extension studies.

**Methods:** These were open-label, 52- and 26-week, flexible-dose studies (study 1 [NCT01447576]: 0.25-3 mg/day; study 2 [NCT01360866]: 0.5-3 mg/day) with brexpiprazole. Study 1 enrolled de novo patients and patients completing one of the two phase II studies (NCT00797966; NCT01052077) while study 2 enrolled patients completing one of the two pivotal phase III studies (NCT01360645 [1]; NCT01360632 [2]). Study 2 is still ongoing; data presented are based on a data-cut from 15-May-2015.

**Results:** 2084 patients were enrolled (697 from study 1 and 1387 from study 2); 48.8% (1016/2084) completed 52 weeks of treatment. Mean brexpiprazole dose was 1.6 mg/day. 13.9% (291/2084) of the patients had a TEAE leading to withdrawal; most frequent AEs leading to withdrawal (≥1%) were weight increased (3.6%) and depression (1.3%). The two most frequently reported AEs were weight increased (25.5%) and akathisia (10.0%); the AE profile was similar to that observed in the short-term lead-in studies with no indication of an increased incidence over time for any AEs. Mean weight gain was 2.9 kg at week 26 (n=1259) and 3.2 kg at week 52 (n=1015). 30.3% (629/2077) of patients had a weight increase that was ≥7% in body weight. There were small changes in other metabolic parameters.

**Conclusion:** Long-term adjunctive treatment with brexpiprazole was safe and well tolerated. Although increases in body weight were observed over time for some patients, the low incidence of discontinuation among those patients suggests that the weight gain was not treatment-limiting for most patients.

**References**

1. Thase ME et al. J Clin Psychiatry. 2015; 76:1224–31
2. Thase ME et al. J Clin Psychiatry. 2015; 76:1232–40

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**PS156**

**Adjunctive brexpiprazole, a novel effective strategy for treating Major depressive disorder?: Systematic review and Meta-analysis**

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**Abstract**

**Background:** Brexpiprazole is the newly approved atypical antipsychotics for the adjunctive therapy to antidepressant treatment in major depressive disorder. Brexpiprazole is serotonin-dopamine activity modulator with dopaminergic partial agonist activity like aripiprazole but has lower affinity to D2 and higher affinity to 5-HT1A and 5-HT2A. These pharmacodynamic differences make expectation of lower akathisia and distinct characteristic on management of depression. This systematic review and meta-analysis aimed to evaluate the efficacy and tolerability of brexpiprazole in adjunctive use in depression.

**Methods:** Article searching was performed in PubMed, Cochrane library database, EMBase, Google scholar and Clinicaltrials.gov. (searching was limited to completed studies) from inception to January 14th 2016, using search terms: “depression” or “depressive (for including depressive illness or major depressive disorder)” and “brexpiprazole” or “OPC-34712”. Statistical analysis for acquiring heterogeneity of studies and pooled value were performed using RevMan 5.3.

**Results:** 2 journal articles and 13 conference abstracts relevant with 9 completed clinical trials were found. Among 2 more registered completed trials, one had results on online but the other had not. 4 randomised controlled trials used for meta-analysis of brexpiprazole 1–3 mg and yielded superior efficacy to placebo with pooled mean difference of change in MADRS and HAM_D (-1.89, 95% CI= -2.59 – -1.18, p-value<0.00001; -2.13, 95% CI= -3.28 – -0.99, p-value=0.003). The risk of akathisia and weight increase was higher in brexpiprazole 1–3 mg with risk ratio, 3.39 (95% CI= 2.08 – 5.51) and 4.36 (95%CI= 2.45–7.77) respectively.

**Conclusion:** Overall, brexpiprazole shows good efficacy and safety profile in adjunctive treatment for depression.

**Keywords:** Brexpiprazole; OPC-34712; Major depressive disorder; Efficacy; Tolerability

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**PS157**

**Impact of benzodiazepine on cognition of remitted depression**

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**Abstract**

It has been widely reported regarding relationship between depression and cognitive function. Benzodiazepines (BZD) has been reported that there is risk by which it itself has an influence on the cognitive function. The aim of the present study was to clarify whether BZD influenced to the cognitive impairment in remitted depression.

Patients had previously met DSM-IV criteria for Major Depressive Disorder (MDD), who had not taken tricyclic antidepressants (TCA). At immediately after remission defined as a score ≤ 7 on HAM-D, we divided MDD patients into taking or not taking BZD. BZD group (n = 98) and non-BZD group (n = 89) and healthy controls (n = 311) were recruited. Cognitive functions were measured using the Logical Memory (LM) subtest of the Wechsler Memory Scale Revised (WMS-R) and Stroop Color and Word Test (Stroop). And score of cognitive tests were compared between the three groups.

In results, scores of LM and Stroop in BZD and non-BZD groups were decreased significantly compared with those in healthy subjects group (p < 0.001, Mann-Whitney U). However, in comparison between BZD and non-BZD groups on Stroop, there was not significant difference. For multiple regression analysis, scores of LM and Stroop were not affected with daily doses of BZD.

In conclusions, cognitive function in patients treated with BZD may not be different from those in patients treated without BZD. Thus, our findings may suggest that cognitive function in even medicated depression without BZD did not improve to healthy levels after remission.

**PS158**

Factors associated with relapse after a response to electroconvulsive therapy in unipolar versus bipolar depression

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**Abstract**

**Background:** Despite the effectiveness of electroconvulsive therapy (ECT) treatment for depression, there is a high rate of relapse, even with maintenance pharmacotherapy. This study investigated factors associated with a risk of relapse in mood disorders after a response to ECT.

**Method:** The records of 78 patients with mood disorders (46 unipolar depression, 32 bipolar depression) who received and responded to an acute ECT course were retrospectively reviewed. Patients with records for at least one year were included. An association between clinical variables and relapse after a response to acute ECT was analyzed. Relapse was defined as a Clinical Global Impressions Improvement score ≥ 6 or a psychiatric rehospitalization.

**Results:** After one year, the relapse-free rate of all patients at one year was 44.9% and there were no significant difference between patients with either unipolar or bipolar depression who were relapse-free (unipolar: 45.7%, bipolar: 43.7% P = 0.868). The mean duration until relapse was 21.6±11.2 months (unipolar: 22.0±11.6 months, bipolar: 20.9±10.8 months, P = 0.796). Maintenance pharmacotherapy with valproate in patients with unipolar depression was associated with a lower risk of relapse compared to patients without valproate treatment (multivariate analysis, hazard ratio: 0.080; P = 0.025). Lithium treatment was associated with a tendency for a lower risk of relapse (hazard ratio: 0.413; P = 0.091). Female sex was associated with a tendency for an increased risk of relapse (hazard ratio: 2.517; P = 0.089). For bipolar depression, quetiapine treatment tended to lower the risk of relapse (hazard ratio: 0.144; P = 0.081).

**Limitation:** The current findings were based on a limited sample size and retrospective.

**Conclusions:** Although the relapse-free rate was similar between unipolar and bipolar depression, effective maintenance pharmacotherapy differed. In unipolar depression, valproate could be effective in preventing relapse after an ECT.

**PS159**

Altered serum levels of matrix metalloproteinase-2, -9 in response to electroconvulsive therapy for mood disorders.

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**Abstract**

**Background:** Mood disorders are being increasingly recognized as having a strong association with chronic inflammatory states. Matrix metalloproteinases (MMPs) and tissue inhibitors of matrix metalloproteinases (TIMP) are inflammation-related molecules. The major MMPs, MMP-2, -9, and TIMP-2, -1, are inflammatory-related molecules that likely have key roles in mood disorders. The current study sought an association between mood disorders and systemic levels of MMPs and TIMPs.

**Methods:** Serum was obtained from patients with mood disorders (MD) (N = 21) and patients with schizophrenia (SCZ) (N = 13) scheduled to undergo electroconvulsive therapy (ECT). Serum was also obtained from healthy controls (N = 40). Clinical symptoms were assessed by the Hamilton Rating Score for Depression and the Brief Psychiatric Rating Scale. Serum levels of MMPs and TIMPs were quantified by enzyme-linked immunosorbent assay.

**Results:** The serum levels of MMP-2 in MD patients, but not in SCZ patients, prior to the first ECT session (baseline), were significantly lower than those of healthy controls. At baseline, levels of MMP-9 and TIMP-2, -1 were not different between patients with MD, SCZ and healthy controls. After a course of ECT, MMP-2 levels were significantly increased in MD patients but MMP-9 levels significantly decreased in both MD and SCZ patients. In MD patients, there was a significant negative correlation between depressive symptoms and serum levels of MMP-2 and a positive correlation between depressive symptoms and MMP-9. In addition, alterations of serum levels of MMP-2 and 9 were significantly correlated each other and were associated with certain depressive symptoms.

**Conclusion:** A change in inflammatory homeostasis, as indicated by MMP-2 and MMP-9, could be related to mood disorders and these markers appear to be sensitive to ECT.