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The influence of subsyndromal mood symptoms (SSMS) on cognition and psychosocial functioning of euthymic bipolar patients remains unclear. Viewpoints vary from minor to major influence of SSMS, but seem to be dependent on the methodological choices of the respective researchers. The present study evaluates the relationship between SSMS and cognitive or psychosocial functioning. 16 euthymic patients with bipolar (I: n= 10; II: n= 6) disorder according to DSM-IV criteria were included. SSMS were measured using the MOODS-SR. Cognitive functioning was measured using STROOP, Trail Making Task, WMS-R visual memory subtests, CVLT, WCST, BADS, NART, amongst others. Psychosocial functioning was determined using the GVSG-45, and the Rand-36. Number of bipolar mood symptoms significantly predicted psychosocial functioning. Post-hoc analyses revealed this effect was greatest for the number of depressive symptoms. To our surprise, cognitive functioning had no significant relation to number of mood symptoms or psychosocial functioning. Although the study has several limitations, our results may imply careful detection of subsyndromal depressive mood symptoms in recovered bipolar patients, as these symptoms may typically be responsible for lowered psychosocial functioning and well-being.

P0154

Functional, social and labour impact of depressive symptoms in bipolar disorder (Sindepres study)

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Background and Aims: The impact of depressive symptoms in stability phases on bipolar disorder outpatients' functional aspects could be important to determine if they are impaired and their treatment requirements. Our aim is to describe functional impact and social adjustment in stable BD, regarding present subclinical depressive symptoms.

Methods: Crossectional, prospective, 16-week study of a cohort of 761 BD patients included by 94 investigators. Clinical stability was assessed at baseline and week 16, with the Clinical Global Impression scale for BD (CGI-BP-M), depressive symptoms at baseline with the Hamilton Depression Rating Scale (HDRS), the Montgomery-Asberg Scale (MADRS) and with the self-applied Center for Epidemiologic Studies-Depression Scale (CES-D). Functional status was evaluated with Social and Occupational Functioning Assessment Scale (SOFAS) and Social Adaptation Self-evaluation Scale (SASS).

Results: Depressive symptoms were detected: mean scores on the HDRS 3.7 (SD 3.1), MADRS 4.9 (SD 4.5) and CES-D 15.2 (SD 9.9) scales. On EEASL mean was 79.5 (SD 12.7), showing a slight decline in social-labour activity and poor social adjustment; SASS mean was 37.5 (SD 7.9). 3.4% of the sample (95%CI 2.0-4.8) presented mild depression with moderate functional impact. The presence of depressive symptoms is related to social-labour functional impact and social maladjustment. The highest correlation coefficients are seen between EEASL and MADRS (r= -0.54, $p<0.0001$) and between SASS and CES-D (r=-0.47, $p<0.0001$).

Conclusions: Depressive symptoms on BD outpatients may result in a decline in social-labour functionality and social maladjustment. Self-applied tests performed during follow-up provide important information about patient's functionality.

P0155

Maintenance treatment in bipolar I disorder with Quetiapine in combination with Lithium/Divalproex: A placebo-controlled, randomized trial (North American trial D1447C00127)

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Background and Aims: To examine the long-term efficacy and safety of quetiapine in combination with lithium (Li) or divalproex (DVP) in the prevention of recurrent mood events (manic, mixed, or depressed).

Methods: Patients with bipolar I disorder (DSM-IV, most recent episode manic, mixed or depressed) received open-label quetiapine (400–800 mg/day; flexible, divided doses)+Li/DVP (target serum concentrations 0.5–1.2 mEq/L and 50–125 μg/mL) for up to 36 weeks to achieve ≥12 weeks of clinical stability. Patients were subsequently randomized to double-blind treatment with quetiapine (400–800 mg/day)+Li/DVP or placebo+Li/DVP for up to 104 weeks. Primary endpoint was time to recurrence of any mood event defined by medication initiation, hospitalization, YMRS or MADRS scores ≥20 at two consecutive assessments, or study discontinuation due to a mood event.

Results: 1953 patients entered the stabilization phase and 623 were randomized and received ≥1 dose of study medication. Rates of recurrence of a mood event were 20.3% (63/310) vs 52.1% (163/313) for quetiapine and placebo groups, respectively, a risk reduction of 68% (HR 0.32; $P<0.0001$). Risk reductions were similar for manic and depressed events (HRs 0.30 and 0.33, respectively; $P<0.0001$). Safety data were consistent with the recognized safety profile of quetiapine. However, a greater incidence of blood glucose ≥126 mg/dL was observed in the quetiapine treatment group.

Conclusions: Maintenance treatment with quetiapine+Li/DVP was significantly more effective than placebo+Li/DVP in increasing the time to recurrence of a mood event in stable patients with bipolar I disorder.

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P0156

Efficacy and safety of Quetiapine in combination with Lithium/Divalproex as maintenance treatment for bipolar i disorder (international trial D1447C00126)

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Background and Aims: An international, randomized, double-blind, parallel-group study was designed to determine the efficacy and safety of quetiapine+Li/DVP compared with placebo+Li/DVP in

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the prevention of recurrent mood events (manic, mixed, or depressed) in patients with bipolar I disorder.

Methods: Patients with bipolar I disorder (DSM-IV, most recent episode manic, mixed or depressed) received open-label quetiapine (400–800 mg/day; flexible, divided doses) plus Li/DVP (target serum concentrations 0.5–1.2 mEq/L and 50–125 μg/mL, respectively) for up to 36 weeks to achieve at least 12 weeks of clinical stability. Patients were subsequently randomized to double-blind treatment with quetiapine (400–800 mg/day) plus Li/DVP or placebo+Li/DVP for up to 104 weeks. Primary endpoint was time to recurrence of any mood event defined by medication initiation, hospitalization, YMRS or MADRS score ≥20 at two consecutive assessments or at final assessment if the patient discontinued, or study discontinuation due to a mood event.

Results: 1461 patients entered the stabilization phase and 703 (48%) were randomized to double-blind treatment receiving at least one dose of study medication (ITT population). A markedly lower proportion of patients had a mood event in the quetiapine+Li/DVP versus placebo+Li/DVP group (18.5% vs 49.0%, respectively), with a risk reduction of 72% (hazard ratio 0.28; P<0.0001). The incidence of adverse events was similar between the two treatment groups.

Conclusions: Maintenance treatment with quetiapine+Li/DVP significantly increased the time to recurrence of any mood event compared with placebo+LI/DVP. Long-term treatment with quetiapine was generally well-tolerated.

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P0157

Why clinicians maintain antidepressants in some patients with acute mania? Hints from a large, observational study (EMBLEM)

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Aim: Antidepressants are recommended to be withdrawn during a manic episode. This analysis explored the characteristics of patients receiving antidepressants during an acute manic episode in the context of a large, observational study.

Method: EMBLEM (European Mania in Bipolar Longitudinal Evaluation of Medication) is a 2-year prospective observational study of acute mania/mixed mania. Of 2416 patients, 345 (14%) were taking an antidepressant (AD) and 2071 (86%) were not (NAD) during acute mania. Demographic and clinical variables were collected at baseline and at outpatient visits up to 2 years. Illness severity was measured using Clinical Global Impressions–Bipolar Disorder (CGI-BP), 5-item Hamilton Depression Rating Scale (HAM-D-5), and Young Mania Rating Scale (YMRS). Logistic regression analysis was used to identify variables associated with AD use.

Results: AD use varied across countries (p<0.05), more use with mixed episodes (p<0.001), rapid cyclers (p=0.02), more previous depressive episodes (p<0.001) and higher HAM-D-5 severity at baseline (p<0.001) but less use with higher education (p=0.029), YMRS (p=0.022), CGI-BP overall (p=0.006) severity and inpatients at baseline (p<0.001). There were no differences in alcohol abuse or suicide attempts. Depression recurrence rates were significantly higher with AD (p<0.001).

Conclusions: The EMBLEM study suggests that patients with mania receiving antidepressants are more likely to be outpatients with mixed mania or rapid cycling, and have a higher risk of depressive recurrence during follow-up. Clinicians seem to maintain antidepressants in manic patients to address depressive features during mania and prevent further depressive episodes.

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P0158

Aripiprazole in combination with Lithium/Valproate in bipolar mania (CN138-134)

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Background and Aims: To evaluate the efficacy, safety and tolerability of aripiprazole plus valproate/lithium in the treatment of patients with bipolar I mania partially non-responsive to lithium or valproate monotherapy.

Methods: This multicentre, randomized study included patients with bipolar I disorder (manic/mixed episode, with/without psychotic features). Partial non-responders with therapeutic lithium (0.6–1.0 mmol/l) or valproate (50–125 μg/ml) levels were randomized (2:1) to double-blind combination aripiprazole (aripiprazole [15–30 mg/day] + lithium/valproate; n=253) or placebo + lithium/valproate (n=131). The primary endpoint was mean change from baseline in YMRS Total Score at Week 6 (LOCF).

Results: The aripiprazole combination therapy demonstrated significant improvement from baseline in the YMRS Total score versus placebo + lithium/valproate at Week 1 and all subsequent visits (all p<0.05) up to Week 6 (−13.3 vs. −10.7, p=0.002; LOCF). Significant improvements from baseline to Week 6 were observed with aripiprazole vs. placebo + lithium/valproate in CGI-BP-S (mania) score (−1.9 vs. −1.6; p=0.014; LOCF) and the LIFE-RIFT score (−1.76 vs. −0.99; p=0.046; LOCF). At endpoint, aripiprazole plus lithium/valproate was associated with significantly greater remission rate (YMRS Total score ≤12) and response rate (≥50% improvement from baseline in YMRS Total) than placebo + lithium/valproate. Similar percentages of patients had clinically relevant weight gain (aripiprazole + lithium/valproate vs. placebo + lithium/valproate: 3.0% vs. 3.9%; p=0.718, Week 6, LOCF). Aripiprazole combination therapy was well tolerated.

Conclusions: In patients with bipolar mania, aripiprazole in combination with lithium/valproate is an effective and well-tolerated treatment that improves psychosocial functioning.

P0159

Metabolic syndrome in patients with bipolar disorder

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