developing mania. However, the extent to which this depends on what type of antidepressant is prescribed remains unclear.

*Aims* To investigate the association between different classes of antidepressants and subsequent onset of mania/bipolar disorder in a real-world clinical setting.

*Methods* Data on prior antidepressant therapy were extracted from 21,012 adults with unipolar depression receiving care from the South London and Maudsley NHS Foundation Trust (SLaM). multivariable Cox regression analysis (with age and gender as covariates) was used to investigate the association of antidepressant therapy with risk of developing mania/bipolar disorder.

*Results* In total, 91,110 person-years of follow-up data were analysed (mean follow-up: 4.3 years). The overall incidence rate of mania/bipolar disorder was 10.9 per 1000 person-years. The peak incidence of mania/bipolar disorder was seen in patients aged between 26 and 35 years (12.3 per 1000 person-years). The most frequently prescribed antidepressants were SSRIs (35.5%), mirtazapine (9.4%), venlafaxine (5.6%) and TCAs (4.7%). Prior antidepressant treatment was associated with an increased incidence of mania/bipolar disorder ranging from 13.1 to 19.1 per 1000 person-years. Multivariable analysis indicated a significant association with SSRIs (hazard ratio 1.34, 95% CI 1.18–1.52) and venlafaxine (1.35, 1.07–1.70).

*Conclusions* In people with unipolar depression, antidepressant treatment is associated with an increased risk of subsequent mania/bipolar disorder. These findings highlight the importance of considering risk factors for mania when treating people with depression.

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## EW448

## Characterization of agomelatine-induced liver injury, incidence and risk factors: A pooled analysis of 7605 treated patients

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*Introduction/objective* The hepatic safety of agomelatine was assessed in 49 phase II and III studies. The aim was to analyze the characteristics of patients who developed an increase in transaminases whilst taking agomelatine.

*Method* A retrospective pooled analysis of changes in serum transaminase in 7605 patients treated with agomelatine (25 mg or 50 mg/day) from 49 completed studies was undertaken. A significant increase in serum transaminase was defined as > 3-fold the upper limit of normal (> 3 ULN). Final causality was determined in a case-by-case review by five academic experts.

*Results* Transaminase increased to > 3 ULN in 1.3% and 2.5% of patients treated with 25 mg and 50 mg of agomelatine respectively, compared to 0.5% for placebo. The onset of increased transaminases occurred at < 12 weeks in 64% of patients. The median time to recovery (to ≤ 2ULN) was 14 days following treatment withdrawal. Liver function tests recovered in 36.1% patients despite the contin-

uation of agomelatine, suggesting the presence of a liver adaptive mechanism. Patients with elevated transaminases at baseline, secondary to obesity and fatty liver disease (NAFLD), had an equally increased risk of developing further elevations of transaminases with agomelatine and placebo. This reflects the widespread fluctuations of serum transaminases in patients with NAFLD.

*Conclusions* The overall incidence of abnormal transaminases was low and dose dependent. No specific population was identified regarding potential risk factors. Withdrawal of agomelatine led to rapid recovery, and some patients exhibited an adaptive phenomenon. The liver profile of agomelatine seems safe when serum transaminases are monitored.

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## EW449

## Hospital admissions and direct costs: A comparative study between paliperidone palmitate and oral antipsychotics

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*Introduction* The total costs of schizophrenia increased to 2576 million Euros in 2013 in Spain, or 2.7% of the annual cost of health services. The hospitalizations, along with other intermediate resources, such as Day Hospital, etc., significantly contribute to the increase of economic burden. In Spain, the average hospital stay of schizophrenic patients is 18.24 days, totalling to an average cost of 6,753 Euros/patient (370.23 Euros/patient/day).

*Material and methods* The sample selected included patients from both sexes, aged between 18 and 65 years old, with diagnostic criteria of schizophrenia (according to DSM-IV and ICD-10), admitted in the Mental Health Hospital Unit (MHHU), Úbeda between 2012 and 2013, with registered visits of at least 2 outpatient visits or 1 hospitalization related to the schizophrenia diagnosis ($n = 48$).

*Results* After the start of treatment with the injectable antipsychotic drug of prolonged duration, the number of patients that required hospitalization for any psychiatric motive went from 24 patients (49.7%) to 11 patients (22.4%; $P < 0.001$). The patients who started treatment with PAP during hospitalization had an average stay of 15.7 days, as compared to 18.24 days of average hospital stay due to schizophrenia in Spain. The direct costs of hospitalization stays due to psychiatric reasons decreased from 162,071.88 Euros to 74,282.95 Euros ($P < 0.001$).

*Conclusions* This observational study shows us that the treatment with PAP reduced the average length of the hospital stay, and resulted in a decreased percentage of re-admissions as compared to oral treatments for schizophrenia. These data led to savings of more than 50% of the direct costs of hospitalization.

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