

significantly more effective than placebo in the overall population, and also in the severely depressed population (HAMD score >25, and with a combination of HAMD score of 25 or more and a CGI score of 5 or more;  $P < 0.05$ ). Similarly, in a trial in elderly patients aged 60 and above, agomelatine was shown to be effective in the more severely depressed patients. Another clinical trial demonstrated the same percentage of responders and remitters between venlafaxine (150 mg/day) and agomelatine (50 mg/day); the first results will be presented during the symposium. Updated data concerning the efficacy of this innovative melatonergic agonist and 5-HT<sub>2C</sub> antagonist antidepressant will be presented as well its action on anxiety symptoms and sleep within depression.

### LS-03-04

Sleep as a marker of disrupted circadian rhythms in depression

C. Guilleminault. *Stanford Sleep Disorders Center, Stanford, USA*

Sleep is one of the circadian rhythms often disturbed in depressed patients. A resetting of these disturbed rhythms is known to have beneficial effects on depressive states, with a normal circadian profile being restored after recovery. Agomelatine is a new antidepressant with an entirely innovative mode of action: it is the first melatonergic agonist antidepressant. Agomelatine is effective for the treatment of major depressive disorder, with particular advantages in improving sleep of depressed patients, without being sedative or increasing daytime clumsiness. Analysis of the HAMD sleep item results of efficacy studies showed agomelatine to be better than placebo on all three phases of sleep, early insomnia ( $P < 0.001$ ), middle insomnia ( $P = 0.015$ ), and early waking ( $P = 0.006$ ), with a similar treatment size effect. Furthermore, using the Leeds Sleep Evaluation Questionnaire in clinical trials, agomelatine significantly improved the ability to get off to sleep and improved the quality of sleep. This effectiveness was seen versus placebo ( $P < 0.001$ ) and SSRIs ( $P < 0.001$ ). In order to confirm the subjective sleep improvements, a specific polysomnography study was performed to examine the effect of agomelatine on sleep architecture of depressed patients. There were clear changes in sleep structure and NREM sleep stage distribution following treatment. Agomelatine appears as an innovative treatment for depression, because of its chronobiotic activity regulating circadian rhythms, and its interaction with the serotonergic system. The ability of agomelatine to relieve sleep complaints, without being sedative, is a key advantage for depressed patients, who frequently suffer from sleep disturbances associated with their depression.

### LS-03-05

Benefits and tolerability evaluation of agomelatine: A new approach to the treatment of depressed patients

S. Montgomery. *London, United Kingdom*

Agomelatine is a new antidepressant, being the first melatonergic (MT<sub>1</sub> and MT<sub>2</sub> receptor) agonist antidepressant. Its antidepressant efficacy at a mean dose of 25 mg daily has been shown in a dose-ranging study performed in major depressive disorder (MDD).<sup>1</sup> Agomelatine's safety and tolerability has been examined across a wide range of studies. The pharmacological profile of agomelatine differs from standard antidepressants, and it has been shown to lack the typical antidepressant side effects (ie, gastrointestinal disorders, weight gain, insomnia). The effect of agomelatine on sexual

function was compared with venlafaxine in a specific study using the SEX-FX scale in remitted MDD patients after 12 weeks of treatment. Significantly fewer remitters experienced sexual dysfunction in the agomelatine group than in the venlafaxine group measured on desire-arousal ( $P < 0.05$ ) and orgasm ( $P < 0.01$ ) dimensions. There are concerns about drug discontinuation syndromes, associated mainly with SSRIs and SNRIs. A double-blind study with discontinuation of either agomelatine or paroxetine on placebo or continued medication was performed.<sup>2</sup> After one week of treatment discontinuation, no signs of discontinuation symptoms were observed in the agomelatine group compared with placebo, whereas the cessation of paroxetine treatment was associated with significant discontinuation symptoms. Agomelatine is an interesting antidepressant that is effective in both moderate and severe depression; it improves sleep without being sedative, and its efficacy is not compromised by sexual side effects, tolerability problems, or discontinuation symptoms.

### References

- Lêo H, Hale A, D'haenen H. *Int Clin Psychopharmacol*. 2002;17:239-247.  
 Montgomery SA, Kennedy SH, Burrows GD, Lejoyeux M, Hindmarch I. *Int Clin Psychopharmacol*. 2004;19:271-280.

### Conclusion

D. Naber. *UKE UniversitätsKH Eppendorf Psychiatrische Klinik, Hamburg, Germany*.

Monday, April 4, 2005

## LS-04. Satellite symposium: Overcoming common barriers to treatment adherence in bipolar disorder

Supported by an unrestricted educational grant from Eli Lilly

Chairperson(s): Siegfried Kasper (Wien, Austria)  
 12.30 - 14.00, Holiday Inn - Hall 1

### LS-04-01

Medical comorbidities and bipolar disorder

S. Kasper. *Medizinische Universität Allgem. Psychiatrie, Wien, Austria*

Nearly 20% of all patients with bipolar disorder have a comorbid illness. Younger patients are more likely to have a comorbid psychiatric illness, while comorbid, physical illness is a greater problem in the elderly. The prevalence of comorbidity associated with bipolar disorder creates a unique diagnostic and treatment challenge. Illnesses such as epilepsy and cardiovascular disease are also strongly associated with bipolar disorder. This symposium will review the methods of assessing comorbid illnesses that may disguise the presence of, as well as affect the course and prognosis of, bipolar disorder. Comorbid illnesses also impact treatment; therefore, strategies for selecting appropriate treatment options will be discussed.

**LS-04-02**

Drug abuse and bipolar disorder

S. Stakowski. *Germany*

In the 1920s, Kraepelin recognized the frequent occurrence of alcoholism in bipolar disorder. The incidence of comorbid alcohol and substance abuse with bipolar disorder ranges from 46%–76% compared to only 14% in the population as a whole. Thirty-four percent of bipolar patients with a history of suicide attempts have a positive family history of drug abuse. Alcoholism appears to be more prevalent in family members of bipolar adults and children. The severity of mania episodes, but not depressive episodes, is associated with drug abuse. Substance abuse is associated with medication non-compliance, more mixed or dysphoric mania, and more hospitalizations. Correct diagnosis needs to be a priority since drugs of abuse, particularly stimulants are associated with symptoms similar to those of mania or even psychosis.

**LS-04-03**

Depression and bipolar disorder

H.-J. Möller. *Ludwig-Maximilians-Universität Klinik für Psychiatrie, München, Germany*

Bipolar depression is difficult to diagnose and challenging to treat. Sixty percent of patients are misdiagnosed an average of 3.5 times before receiving the appropriate diagnosis. Most commonly, patients are misdiagnosed as having unipolar depression, anxiety disorder, and schizophrenia. Methods of distinguishing bipolar depression from other psychiatric illnesses will be presented. Past history, phenomenology, family history, and treatment response will all be characterized as indicators of the presence of bipolar disorder. Differential diagnosis is imperative in choosing therapy. One focus will be the available treatment options, as well as the appropriate use of antidepressants.

Monday, April 4, 2005

**LS-02. Satellite symposium: Antidepressant myths and facts: Do the data reflect clinical reality?****Supported by an unrestricted educational grant from Pfizer Inc.**

*Chairperson(s):* David Sheehan (Tampa, USA)  
12.30 - 14.00, Gasteig - Philharmonie

**Chair's introduction**D. Sheehan. *University of South Florida College of Medicine, Tampa, USA***LS-02-01**

Diagnosis and treatment of spectrum depression and anxiety disorders

G. Cassano. *University of Pisa Dept. of Psychiatry, Neurobiol., Pisa, Italy*

Diagnosis of psychiatric disorders is made according to fulfilment of the criteria defined by the current editions of the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) or the International Classification of Diseases (ICD). While there is no doubt that these categorical diagnostic tools are simple and reliable, they have their limitations, since the symptomatology and response to treatment varies between patients. Failure to recognize and manage residual, comorbid, or subthreshold spectrum features may explain continued impairment, even when the core condition has been well treated. An alternative approach, which may better capture an individual's condition, may be the consideration of a 'spectrum' of psychiatric illness. This would encompass various psychiatric symptoms from depression to anxiety, somatic symptoms such as pain, personality traits, and behavioural features related to an established DSM-IV disorder construct. Unexplained somatic symptoms, such as headache and bodily weakness, play an important role in the manifestation of mood disorders. Unfortunately, painful physical symptoms are usually rarely detected. This spectrum approach to diagnosis could be used to optimize management strategies and monitor the course of illness. Community patients presenting with panic disorder, social phobia, or generalized anxiety disorder (GAD) have high rates of lifetime depression comorbidity of approximately 50%. Psychiatric comorbidity is frequent in all age groups, and is associated with increased severity of illness, poor social function, increased somatic symptoms, and greater suicidality. It is also linked to poor treatment outcome, possibly resulting from delayed or diminished response to treatment, or reduced compliance. Although highly prevalent, comorbid depression and anxiety is underdiagnosed and undertreated despite the availability of effective therapies. There is therefore a need to raise awareness among physicians to ensure optimal treatment for patients, and to overcome public misconceptions regarding psychiatric disorders and medications. Clinical trials of antidepressant efficacy in anxiety or depression often exclude patients with psychiatric comorbidity. This presentation will review recent studies demonstrating the efficacy of selective serotonin reuptake inhibitors (SSRIs) and serotonin/norepinephrine reuptake inhibitors (SNRIs) in patients with a variety of comorbid psychiatric disorders, including major depressive disorder comorbid with panic disorder, obsessive-compulsive disorder, or GAD. Data regarding efficacy in post-traumatic stress disorder (PTSD) comorbid with depression or anxiety, and in anxious depression, will also be considered. These studies indicate that some antidepressants are as effective and well tolerated in patients with psychiatric comorbidity as in single mood and anxiety disorders. In summary, this presentation will explore the use of a spectrum model for diagnosis, consider the particular challenges of diagnosis and treatment of psychiatric comorbidity, and review clinical study data evaluating the efficacy of antidepressants in treating patients with comorbid psychiatric disorders.

**LS-02-02**

The importance of actively treating depression in medically ill patients

R. Krishnan. *Duke University Dept. of Psychiatry, Durham, USA*

Depression occurs at a considerably higher rate in patients with medical illness compared with healthy individuals; its prevalence ranges from 10% to 50% in medically ill patients. Comorbid depression is associated with greater physical impairment and with