

ventricular brain ratio) may be more pronounced in patients who have delayed onset of treatment.

Finally, there is the issue of compliance. It has been repeatedly demonstrated that multiple relapses are detrimental to the course of illness. Enhancing treatment compliance, particularly in young schizophrenic patients, may be essential in determining the course of illness. Side effects are a major cause of noncompliance in schizophrenic patients. Therefore, new medications that are better tolerated than the typical antipsychotics may be important assets that the physician can use to improve the course of illness in schizophrenia.

### Lilly-SAT1-2

#### CHALLENGES IN PATIENT MANAGEMENT

David Pickar. *Experimental Therapeutics Branch, Division of Intramural Research Program, National Institute of Mental Health, NIH, Uniformed Services University of the Health Sciences, Bethesda, Maryland, USA*

The introduction of the atypical antipsychotic, clozapine, signaled a major advance in the pharmacotherapy of schizophrenia. The subsequent new generation of atypicals (e.g., olanzapine, risperidone) have gained widespread clinical application and have already made a substantial contribution to improving the outcome of patients with schizophrenia. The neuroscience/pharmacology underpinnings of these compounds have presented new opportunities for further drug development. Coupled with advances in molecular science, including pharmacogenetics, protective genes, etc., the prospects for a further refinement in drugs to treat schizophrenia are excellent.

### Lilly-SAT1-3

#### MOOD AND RELATED SYMPTOMS IN SCHIZOPHRENIA

S.A. Montgomery. *Imperial College School of Medicine at St Mary's, London, UK*

Depressive symptoms are frequently found to be part of schizophrenia. Estimates of between 25% and 60% of acute episodes of schizophrenia are associated with depression that often persists after treatment with classical antipsychotics. The depression has a profound effect on the quality of life and is an important predictor of suicide. The depression is often mistakenly confused with the negative symptoms of schizophrenia.

Olanzapine is the most thoroughly studied of the atypical antipsychotics in schizophrenia with associated depressive symptoms. It has been found to produce a significantly better response of the depressive symptoms compared with haloperidol measured on the MADRS.

Classical antipsychotics do not appear to treat the full range of symptoms in schizophrenia, as evidenced by depressive symptoms. Effective treatments like olanzapine should be preferred.

### Lilly-SAT1-4

#### COGNITIVE DEFICITS IN SCHIZOPHRENIA

Alan Breier. *Lilly Research Fellow, Lilly Research Laboratories and Professor of Psychiatry, Indiana University School of Medicine, USA*

Schizophrenia is characterized by cognitive deficits that span several domains and include dysfunction in attention, information processing, memory and executive performance. These deficits are observed in first-degree family members suggesting a heritable component. In addition, cognitive deficits pre-date the onset of

schizophrenia indicating they are core components of schizophrenia and not secondary to medication side effects, positive or negative symptoms. There is a growing body of literature suggesting that cognitive abnormalities predict occupational and social dysfunction and may be a major determinant of long-term outcome. The traditional neuroleptic drugs have proven to be relatively ineffective for these deficits and earlier information suggests the new so-called atypical antipsychotic agents have cognitive properties. One of these agents, olanzapine, selectively increases norepinephrine and dopamine in prefrontal cortex, produces early mediated disruption in information gating, and has mixed effects at the muscarinic M-4 receptor – all preclinical evidence supporting cognitive enhancing potential. Moreover, in a recently completed Canadian multi-center, double-blind, one year comparative trial of olanzapine, risperidone and haloperidol in early phase schizophrenia (Purdon, et al, 1998), olanzapine demonstrated superiority for a number of cognitive domains. The future role of atypical antipsychotics for the treatment of cognitive deficits will be discussed.

### Lilly-SAT1-5

#### QUALITY OF LIFE AND RE-INTEGRATION OF CHRONICALLY ILL PATIENTS

D.A. Revicki. *MEDTAP International, Bethesda, MD, USA*

Schizophrenia is a disabling and chronic disorder associated with severe social, occupational, and quality of life (QOL) impairments. Olanzapine (Olz), an atypical antipsychotic, has demonstrated improved clinical efficacy compared with haloperidol (Hal), but little is known on Olz's impact on QOL and other outcomes. A 6-week clinical trial, with a long-term extension, was conducted to evaluate QOL, occupational, and social outcomes. Patients with schizophrenia or other psychotic disorders were randomized to acute treatment with Olz or Hal and treatment responders entered a 46-week extension. QOL was measured using the Quality of Life Scale (QLS) and SF-36 health survey. During acute treatment, significant improvements were seen in the Olz group compared with the Hal group on QLS total scores ( $p = .005$ ) and SF-36 mental component summary scores ( $p < .001$ ). During the extension, the Olz group continued to show improvements on QLS total scores compared with Hal ( $p = .001$ ). Olz treated patients reported more useful work and employment, compared with Hal treated patients. Olz was effective in improving QOL and other outcomes necessary for re-integration into the community.

---

Eli Lilly & Co.

## Lilly-SAT2. Zyprexa: New advances in the management of bipolar disorders

*Chair:* R Licht (DK)

---

### Lilly-SAT2-1

No abstract received

### Lilly-SAT2-2

#### LITHIUM AND ANTIEPILEPTICS IN THE TREATMENT OF BIPOLAR DISORDER

A.H. Young. *Department of Neurosciences and Psychiatry, University of Newcastle Newcastle NE1 4LP, UK*

The element Lithium was discovered in 1817 and used to treat mood disorders in the 19th century. However, because of deaths