# Agent May Ease Parkinson's Psychosis Symptoms

BY PATRICE WENDLING
*Chicago Bureau*

CHICAGO — The investigational agent pimavanserin appears to lessen the symptoms of psychosis in patients with Parkinson's disease without worsening motor function, according to data from a multicenter randomized phase II trial involving 60 patients.

Pimavanserin is a potent, active 5-hydroxytryptamine 2a ($5\text{-HT}_{2a}$) serotonin receptor antagonist, according to Dr. Revell of Acadia Pharmaceuticals Inc., which sponsored the study. However, it lacks the dopamine receptor ($D_2$) and histamine receptor ($H_1$) binding that are linked to intolerable adverse effects of other antipsychotics. Pimavanserin is being developed as a cotherapy for schizophrenia, as well as for Parkinson's disease psychosis.

**Adverse events commonly experienced with clozapine and quetiapine—such as somnolence, fatigue, and dizziness—were uncommon with pimavanserin.**

Patients in the study had Parkinson's disease and psychosis and received either pimavanserin (n = 29) or placebo (n = 31) on an outpatient basis for 28 days, starting at 20 mg daily on day 1, with dose escalations to 40 mg and 60 mg on day 8 and 15, respectively, depending on individual clinical response.

Patients treated with pimavanserin demonstrated a 40% improvement in the Scale for the Assessment of Positive Symptoms (SAPS) combination score for hallucination and delusion, as compared with an 11% improvement for patients treated with placebo, Dr. Stephen Revell and associates reported in a poster at the 12th International Congress of Parkinson's Disease and Movement Disorders.

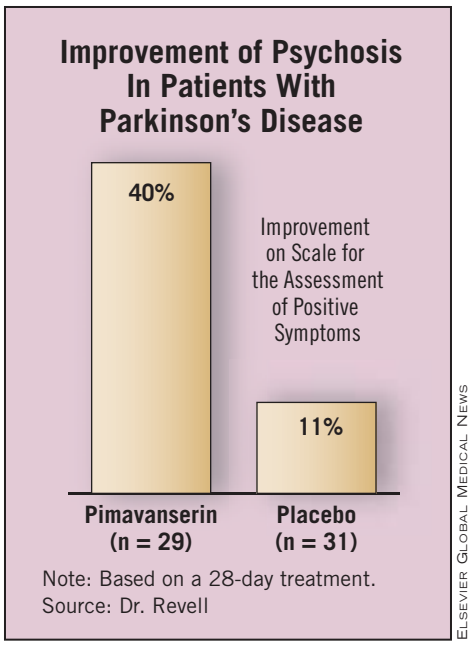
Statistically significant improvements also were observed for patients treated with pimavanserin on the mentation, behavior, and mood part of the Unified Parkinson's Disease Rating Scale (UPDRS).

There was no clinically significant difference between patients treated with placebo vs. pimavanserin in absolute mean change from baseline to day 28 in UPDRS motor scores (–3.05 vs. –1.24) or activities of daily living scores (–2.51 vs. –0.70).

No differences were observed between groups on the Schwab and England Activities of Daily Living Scale part of the UPDRS or the Clinical Global Impression Scale severity of illness subscale.

The most common adverse events in patients treated with pimavanserin were somnolence, edema, and increased blood urea—each occurring in three patients, the authors wrote.

In a second poster presented at the meeting, pimavanserin was well tolerated and did not worsen Parkinsonism symptoms in 39 patients (mean age 72 years) with Parkinson's and psychosis at doses up to 60 mg/day for up to 42 months (mean 14 months). Adverse events commonly experienced with clozapine and quetiapine—such as somnolence, fatigue, and dizziness—were uncommon with pimavanserin, according to Dr. Roger Mills, also of Acadia, who led the industry-sponsored, open-label extension safety study.



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Only one patient who experienced somnolence discontinued pimavanserin treatment. A single case of rhabdomyolysis was the only serious adverse event considered to be possibly treatment-related. ■

# *Tricyclics and SSRIs Show Efficacy for Treatment of Irritable Bowel Syndrome*

BY LISA ZAMOSKY
*Contributing Writer*

SAN DIEGO — There is a strong rationale as well as some evidence supporting the use of tricyclic antidepressants and selective serotonin reuptake inhibitors for the treatment of irritable bowel syndrome, Dr. Lin Chang said at the annual Digestive Disease Week.

Dr. Chang, a gastroenterologist with the Center for Neurovisceral Sciences and Women's Health at the University of California, Los Angeles' division of digestive diseases, discussed the theoretical basis and the available research data supporting the use of selective serotonin reuptake inhibitors and tricyclic antidepressants (TCAs) for treating irritable bowel syndrome.

First, the majority of IBS patients seen in a referral practice—as many as 60%—have some type of psychological disturbance, such as depression, anxiety, personality difficulties, or life stress.

Second, one of the key mechanisms of IBS involves alterations in the brain-gut interaction. As a result, TCAs and SSRIs may be able to change visceral sensitivity and motor activity, or both. Finally, both of these classes of medication appear to help regulate pain.

During her talk, Dr. Chang discussed one of the largest studies on TCAs for the treatment of IBS, in which the investigators evaluated the efficacy of the TCA desipramine in a placebo-controlled 12-week study (Gastroenterology 2003;125:19-31). Patients had moderate to severe functional bowel disorders and most met the criteria for IBS. The researchers started patients at 50 mg of desipramine, moving them up to 100 mg and then 150 mg during the course of the study.

In the IBS patients, 62.5% of those on desipramine had improvement of their symptoms, compared with 37.5% of those on placebo. Only patients who completed treatment were included.

Most patients with IBS have chronic functional abdominal pain that is very difficult to treat, according to Dr. Chang. "Tricyclics can be beneficial in IBS," she concluded, stating that because of their anticholinergic effects, TCAs have been shown to improve IBS symptoms.

Dr. Chang pointed out that the desipramine study, while demonstrating a benefit, utilized a very high dose of TCAs at the outset with patients, something that she finds difficult to implement in practice. "IBS patients have a lot of drug sensitivity, so I start at a lower dose. I tell them that they may not see an effect [right away] but that they may want to start slower and titrate it up. The slower you go, the fewer side effects you'll have."

Dr. Chang also discussed two studies that demonstrated the efficacy of SSRIs in the treatment of IBS. One study compared paroxetine with psychotherapy and usual medical treatment by a gastroenterologist (Gastroenterology 2003;124:303-17). The investigators found that both paroxetine and psychotherapy reduced pain scores and improved health-related quality of life compared with usual medical treatment. This study was the first to show that SSRIs are an effective treatment for functional gastrointestinal disorders.

In the other study, investigators conducted a crossover trial on IBS patients, comparing 6 weeks of treatment with citalopram (3 weeks at 20 mg, 3 weeks at 40 mg) with placebo (Gut 2006;55:1095-103). Following 3 and 6 weeks of treatment, there was significant improvement in the group given citalopram with respect to abdominal pain, bloating, the impact of symptoms on daily life, and overall well-being. The impact on stool pattern, however, was only moderate. "There is evidence, separate from mood, that SSRIs may help GI symptoms," Dr. Chang concluded.

Although literature supporting the use of TCAs and SSRIs is lacking, she said that other medications used for IBS have not been effective and that these medications seem to work. She said she takes care of patients with "very severe" conditions, "which means you have to think outside of the box; you have to be creative." ■

# Insomnia Is Common During Chemotherapy

BY KERRI WACHTER
*Senior Writer*

CHICAGO — The prevalence of insomnia is roughly three times greater among cancer patients than it is among the general population, according to a secondary analysis of more than 500 patients.

The prevalence of insomnia that meets clinical criteria was 45.6% among cancer patients receiving chemotherapy, which compares with 19% in the general population. An additional 35% of cancer patients had insomnia symptoms, compared with 15% in the general population, reported Oxana Palesh, Ph.D., a radiation oncologist at the University of Rochester (N.Y.), at the annual meeting of the American Society of Clinical Oncology.

Roughly 80% of the patients continued to have insomnia problems throughout chemotherapy. "So insomnia does not go away on its own," she said.

The researchers also found that the prevalence of insomnia was greatest among lung cancer patients (*P* less than .05). In addition, younger patients tended to have more insomnia (*P* less than .05). The researchers found no difference in the prevalence of insomnia between male and female cancer patients.

For the original study, 832 cancer patients were assessed during chemotherapy cycles 1 and 2.

Those found to have fatigue (547 patients) were randomized to receive either 20 mg paroxetine or placebo. Insomnia was assessed using the Hamilton Rating Scale for Depression (cycles 1, 2, 3, 4), and depression was assessed using the Center for Epidemiologic Studies–Depression scale. Fatigue was assessed using the Fatigue Symptom Checklist and the Multidimensional Assessment of Fatigue.

Patients were mostly female (72%) and white (89%), with a mean age of 57 years. Half had breast cancer, and overall 64% were undergoing adjuvant therapy. Fatigue and depression data were previously reported (J. Clin. Oncology 2003;21:4635-41). Although paroxetine did improve depressive symptoms, it had no effect on fatigue. In this analysis, the researchers reported that paroxetine had no significant effect on insomnia, compared with placebo.

Dr. Palesh reported that she has no relevant financial relationships. ■

Pages 36a—36b