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New Study Data Show Improved Cognitive Function in Elderly Patients Treated with Cymbalta for Depression

Significant Improvements in Depressive Symptoms Seen as Early as One Week

SAN DIEGO, March 7, 2005 /PRNewswire-FirstCall via COMTEX/ -- Elderly patients with depression treated with Cymbalta(R) (duloxetine hydrochloride, pronounced sim- BAWL'-tuh), 60 mg once daily, had twice as much improvement in verbal learning and recalling information than those given a sugar pill, according to new research presented Saturday at the annual meeting of the American Association for Geriatric Psychiatry.

By the end of the eight-week study, Cymbalta-treated patients demonstrated significantly greater improvement in cognition when compared to patients treated with a sugar pill (mean change 1.95 vs. .76). Additionally, 27.4 percent of Cymbalta-treated patients were virtually free of their depressive symptoms, a rate nearly double that seen with a sugar pill (14.7 percent). Significant improvements in depressive symptoms in Cymbalta-treated patients were also seen as early as one week.

Impairment of cognitive functioning is a bigger issue among the elderly with depression than younger adults, one analysis suggests.(i) It is not uncommon for these patients to have short-term memory issues, like forgetting where they placed their keys, or to experience a delay in recalling information.(ii)

"Treating and diagnosing depression in elderly patients can be complicated -- their condition presents differently from younger patients, making it more difficult to diagnose, and their response to medication is less predictable," stated Alan Siegal, MD, associate clinical professor of psychiatry, Yale University. "Depression-related cognitive impairment, along with a greater sensitivity to medication side effects, often make it more difficult for older patients to comply with treatment recommendations."

Depression is a common illness among the aging, affecting two million Americans aged 65 and older.(iii) Often minimized by the patient and their doctor,(iv,v) undiagnosed and untreated elderly depression leads to unnecessary pain and suffering(vi) and increased healthcare costs.(vii) The elderly are predisposed to this condition for many reasons, including failing health, loss of loved ones and frustration with memory loss.(viii)

"Previous clinical trials using other antidepressants in this patient population showed cognitive dysfunction persisted even after the depression had responded to treatment,"(ix) explained Joel Raskin, MD, FRCPC, medical advisor, Eli Lilly and Company. "In this study, significant improvements in both cognition and depression were seen."

Additional study highlights

* By 8 weeks, significantly more patients experienced a response in depressive symptoms to treatment with Cymbalta than to a sugar pill (37.3 vs. 18.6 percent, respectively).

* In comparison with those treated with a sugar pill, significantly fewer Cymbalta-treated patients stopped treatment due to lack of efficacy (9.6 vs. 2.9 percent, respectively).

* Discontinuation rates due to adverse events were similar for both treatment groups (9.7 percent Cymbalta; 8.7 percent placebo).

* The most common adverse events experienced by patients treated with Cymbalta in this study included dry mouth (14.5 percent), nausea (12.6 percent), constipation (10.1 percent), dizziness (8.2 percent), diarrhea (8.2 percent), fatigue (6.3 percent), and somnolence (5.3 percent).

Methods

Data were gathered from 311 patients aged 65 and older who participated in a multicenter, double-blind, placebo-controlled study. After a one-week screening and a one-week, double-blind placebo phase, patients were randomly chosen to receive either Cymbalta 60 mg once daily (n=207) or a sugar pill (n=104) for eight weeks.

Patients then entered a one-week, double-blind discontinuation phase where the dose of the study medication was tapered.

The primary outcome measure was a composite cognitive score based on four tests that measured verbal learning and memory, selective attention and executive functioning. Secondary measures included the Geriatric Depression Scale and the Hamilton Depression Scale (HAMD17). Response in depression symptoms at endpoint was defined as a greater than 50 percent decrease in the HAMD17 Total Score from baseline. Remission of depression symptoms at endpoint was defined as a HAMD17 Total Score of less than 7.

About Cymbalta

Serotonin and norepinephrine are two neurotransmitters, or chemical messengers, believed to help regulate a person's emotions and sensitivity to pain. Research suggests that increasing levels of serotonin and norepinephrine in the brain and spinal cord can reduce the body's sensation of pain from the nerve damage caused by diabetes.

Based on preclinical data, Cymbalta (pronounced sim-BAWL'-tuh) is a balanced and potent reuptake inhibitor of serotonin and norepinephrine.(x) It is indicated in the United States for the treatment of major depression and the management of diabetic peripheral neuropathic pain. The European Commission has also approved duloxetine for the treatment of major depression and moderate-to-severe stress urinary incontinence in adults. As duloxetine has not been studied in children, Lilly discourages its use in those under 18.

Cymbalta should not be confused with Symbyax(TM) (pronounced SIMM-bee-ax), a medicine for bipolar depression also marketed by Lilly. Symbyax is a combination of olanzapine, the active ingredient in Zyprexa(R), and fluoxetine, the active ingredient in Prozac(R). Symbyax is available in capsules of 6 mg/25 mg (olanzapine/fluoxetine), 12 mg/25 mg, 6 mg/50 mg and 12 mg/50 mg. Cymbalta is available in 20 mg, 30 mg and 60 mg capsules.

Important Safety Information

In clinical studies, antidepressants increased the risk of suicidal thinking and behavior in children and adolescents with depression and other psychiatric disorders. Anyone considering the use of Cymbalta or any other antidepressant in a child or adolescent must balance the risk with the clinical need. Patients who are starting therapy should be observed closely. Families and caregivers should discuss with the doctor any observations of worsening depression symptoms, suicidal thinking and behavior, or unusual changes in behavior. Cymbalta is not approved for use in patients under the age of 18.

Patients on antidepressants and their families or caregivers should watch for worsening depression symptoms, unusual changes in behavior and thoughts of suicide, as well as for anxiety, agitation, panic attacks, difficulty sleeping, irritability, hostility, aggressiveness, impulsivity, restlessness, or extreme hyperactivity. Call the doctor if you have thoughts of suicide or if any of these are severe or occur suddenly. Be especially observant at the beginning of treatment or whenever there is a change in dose.

Prescription Cymbalta is not for everyone. People who are allergic to duloxetine hydrochloride or the other ingredients in Cymbalta should not take it. If you have recently taken a type of antidepressant called a monoamine oxidase inhibitor (MAOI), are taking thioridazine or have uncontrolled narrow- angle glaucoma, you should not take Cymbalta. Talk with your doctor before taking Cymbalta if you have liver or kidney problems, glaucoma or consume large quantities of alcohol. Women who are pregnant should talk with their doctor before taking Cymbalta. Breast-feeding while taking Cymbalta is not recommended.

In clinical studies of Cymbalta for depression, the most common side effects were nausea, dry mouth, constipation, decreased appetite, fatigue, sleepiness, and increased sweating. Cymbalta also is approved for the management of neuropathic pain associated with diabetic peripheral neuropathy. In clinical studies of Cymbalta in these patients, the most common side effects were nausea, sleepiness, dizziness, constipation, dry mouth, increased sweating, decreased appetite, and loss of strength or energy. In all clinical trials, most people were not bothered enough by side effects to stop taking Cymbalta.

Your doctor may periodically check your blood pressure. Don't stop taking Cymbalta without talking to your doctor.

For full prescribing information, including Boxed Warning, visit http://www.Cymbalta.com/ .

About Lilly

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of first-in-class and best-in-class pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers -- through medicines and information -- for some of the world's most urgent medical needs. Additional information about Lilly is available at www.lilly.com . P-LLY

This press release contains forward-looking statements about the potential of Cymbalta for the treatment of cognition, in

addition to major depressive disorder, and reflects Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. There is no guarantee that the product will prove to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filings with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

(i) Serby, Michael, et al. "Overview: Depression in the Elderly." The Mount Sinai Journal Of Medicine, Vol. 70 No. 1 January 2003.

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(v) Birrer, Richard B, et al. "Depression in Later Life: A Diagnostic and Therapeutic Challenge." Am Fam Physician 2004;69:2375-82. http://www.aafp.org/afp/20040515/2375.pdf

(vi) Serby, Michael, et al. "Overview: Depression in the Elderly." The Mount Sinai Journal Of Medicine, Vol. 70 No. 1 January 2003. (http://www.mssm.edu/msjournal/70/v70_1_page_39_44.pdf)

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(ix) Nebes RD, Pollock BG, Houck PR, Butters MA, Mulsant BH, Zmuda MD, Reynolds CF 3rd. J Psychiatr Res. 2003 Mar-Apr;37(2):99-108

(x) Bymaster F, Dreshfield-Ahmad L, Threlkeld P, Shaw J, Thompson B, Nelson D, et al. Comparative affinity of duloxetine and venlafaxine for serotonin and norepinephrine transporters in vitro and in vivo, human serotonin receptor subtypes, and other neuronal receptors. Neuropsychopharmacology. 2001;25(6):871-880.

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