Tapentadol ER Effective for Neuropathic Pain

The investigational analgesic also performed well in treating chronic nociceptive pain of osteoarthritis.

BY BRUCE JANCIN

FROM THE EUROPEAN CONGRESS OF RHEUMATOLOGY

ROME — Tapentadol extended release, an investigational centrally acting analgesic, proved effective both for moderate to severe diabetic peripheral neuropathy and for similarly severe chronic nociceptive pain due to osteoarthritis or low-back injury in a series of five phase III clinical trials.

Tapentadol immediate release (Nucynta) has been approved for the treatment of moderate to severe acute pain. The investigational extended release formulation is a twice-daily drug for which a New Drug Application for marketing approval is now under review at the Food and Drug Administration.

Two of the phase III studies were 15-week, double-blind, multicenter trials totaling 2,010 patients with moderate to severe pain due to osteoarthritis of the knee. They were randomized to tapentadol extended release titrated to 100-250 mg b.i.d. or oxycodone controlled release titrated to 20-50 mg b.i.d. over the first 3 weeks or to placebo.

The tapentadol extended release group showed a significant reduction in mean pain intensity scores over the course of 15 weeks compared with placebo in both trials.

The oxycodone controlled release group was significantly better than placebo in only one trial, Dr. Christine Rauschkolb reported.

The diabetic peripheral neuropathy investigation was a double-blind, 15-week, placebo-controlled study in 389 patients.

The placebo group showed significant worsening of average pain intensity over the 15 weeks. There was no change in pain intensity over time in the tapentadol extended release group, which signifies treatment efficacy, said Dr. Rauschkolb of Johnson & Johnson Pharmaceutical Research & Development, Raritan, N.J.

The double-blind, chronic low-back pain study was also 15 weeks in duration. It included 958 patients with moderate to severe pain who were randomized to tapentadol extended release, oxycodone controlled release, or placebo. Both the tapentadol and oxycodone groups experienced significantly reduced pain intensity from baseline through the end of the study, compared with placebo.

The 1-year-long safety study was an open-label trial conducted in 1,117 patients with osteoarthritis or low-back pain.

They were randomized 4:1 to tapentadol extended release at 100-250 mg b.i.d. or oxycodone controlled release at 20-50 mg b.i.d. Mean pain intensity scores improved in the tapentadol extended release group from 7.58 at baseline to 4.37 at 1 year on an 11-point scale, and from 7.61 to 4.52 with oxycodone controlled release. Nausea, vomiting, and constipation were significantly more frequent in the oxycodone controlled release arm.

The extended release tapentadol was at least as effective as oxycodone controlled release, but it was better tolerated and had a lower discontinuation rate (43.5% vs. 61.7%).

In a separate pooled analysis of three randomized, double-blind phase III studies involving 980 patients who received tapentadol extended release for moderate to severe osteoarthritis or low-back pain, 1,001 patients assigned to oxycodone controlled release, and 993 on placebo, the treatment discontinuation rate was highest by far in the oxycodone arm.

The discontinuation rates were 40.6% with placebo, 43.5% with tapentadol extended release, and 61.7% with oxycodone controlled release, reported Dr. Bernd Lange of Grunenthal GmbH, Aachen, Germany.

The bottom line on this extensive randomized trial experience is that tapentadol extended release is at least as effective as oxycodone controlled release for the management of chronic pain at a ratio of approximately 5 mg of tapentadol extended release to 1 mg of oxycodone controlled release. But tapentadol extended release is better tolerated, Dr. Lange said.

Tapentadol has both mu-opioid receptor agonist and noradrenaline reuptake inhibitor actions.

All of the studies were funded jointly by Johnson & Johnson and Grunenthal GmbH. Dr. Rauschkolb is an employee of Johnson & Johnson, and Dr. Lange is an employee of Grunenthal. ■

Type 1 Survival Rates Improve, Though Challenges Remain

BY MICHELE G. SULLIVAN

FROM THE ANNUAL MEETING OF THE AMERICAN DIABETES ASSOCIATION

ORLANDO — Despite a steadily improving mortality picture, patients with childhood-onset type 1 diabetes still faced significantly increased mortality risks in a 40-year prospective follow-up study.

Women were particularly at risk, with a 13-fold greater risk of death than women in the same Pennsylvania community who were free of the disease, Dr. Trevor J. Orchard said at the meeting.

After 30 years, the death rate was 22% in those diagnosed in 1965-1969, and 15% in the 1975-1979 cohort.

DR. ORCHARD

However, the follow-up study did show improving survival rates. After 30 years, the death rate among those diagnosed in the earliest cohort (1965-1969) was 22%. That dropped to 19% in the 1970-1974 cohort, and to 15% in the 1975-1979 cohort.

"We believe this reflects better care, resulting in fewer deaths early in diagnosis and—more recently—lower rates of diabetes complications," Dr. Orchard, professor of epidemiology at the University of Pittsburgh, said in an interview.

"A lot of patients and the public feel that individuals with childhood-onset type 1 have lower life expectancy. These data firmly support that this is rapidly changing, and most people with type 1 diabetes can look forward to a normal life span if they keep their blood glucose and other risk factors under control," he added.

Dr. Orchard presented data collected by his colleague, Aaron Secrest, who is a Ph.D. candidate at the university.

Mr. Secrest used the Allegheny County Type 1 Diabetes Registry as the basis of his analysis. The registry is one of the largest population-based registries of the disease. "It has been used in a number of studies as a representative cohort of the United States," Dr. Orchard noted.

The analysis included a total of 1,075 residents of Allegheny County, Pa., who were diagnosed with childhood-onset type 1 diabetes in 1965-1979. The population was stratified into three time cohorts: those diagnosed in 1965-1969, in 1970-1974, and in 1975-1979, with about one-third of the cohort included in each time period. In all, 48% of the patients were female, and 93% were white; the small percentage of black patients is representative of the county's overall population.

As of January 2008, 19% (202) of registry participants had died—a rate seven times greater than age- and sex-matched people in the general population. Of those 202 participants, 95 were men and 107 were women.

The cumulative survival rates were 98% at 10 years, 93% at 20 years, 81% at 30 years, and 68% at 40 years. "What this tells is that about one-third of people with childhood-onset type 1 diabetes diagnosed in the 1960s will die within 40 years of their diagnosis," Dr. Orchard said.

Although women within the cohort were not significantly more likely to die than men, "striking differences" emerged when the diabetes group was compared to the background population.

"Compared to the standardized mortality rate of the county, women [in the cohort] were 13 times more likely to die, and men were 5 times more likely to die," Dr. Orchard said. The relative mortality differences between cohort and community and the sex differences in relative mortality were highly statistically significant, he said.

Race also factored significantly into the survival curve. "We saw a tremendously high mortality in blacks, such that 30-year survival was down to 57%, compared to 83% in whites," Dr. Orchard said. "However, the standardized mortality ratio for blacks is very much the same [compared with the local county] as it is for whites, illustrating the relatively high mortality rate in the black background community."

There were 32 deaths among black patients—41% of the black cohort. All of the deaths among blacks were directly related to diabetes.

"We noted that as this increase did include both acute and chronic complications of diabetes, it is most likely related to access to care and/or the ability to follow through with that care," Dr. Orchard said.

"The finding that there was no significant difference in the mortality rates compared to the background population suggests that there is a general socioeconomic status situation that affects outcomes in all diseases," he said. ■

VITALS

Major Finding: Patients with childhood-onset type 1 diabetes are living longer than they did 40 years ago, but still face a sevenfold increase in the risk of death, compared with those without the disease.

Data Source: The Allegheny County Type 1 Diabetes Registry consisting of 1,075 subjects diagnosed from 1965 to 1979. Compared with the standardized background mortality rate, women were 13 times more likely to die, and men were 5 times more likely to die.

Disclosures: The National Institutes of Health sponsored the study. Neither Dr. Orchard nor Mr. Secrest reported any financial conflicts.