Extended-Release Viramune Has Comparable Safety and Efficacy to Standard Viramune

July 22, 2010 By Tim Horn

Viramune XR—a once-daily extended-release version of the nucleoside reverse transcriptase inhibitor nevirapine (NNRTI)—is comparable to standard twice-daily dosing of the approved formulation of the drug, according to study results reported Thursday, July 22, at the XVIII International AIDS Conference in Vienna.

Immediate-release Viramune, one 200-milligram (mg) tablet taken twice daily, is the approved dose in the United States. Study results, however, suggest that once-daily Viramune therapy—one 400mg dose of the NNRTI—is possible (though conflicting data exist). Despite that once-daily dosing is not approved by the U.S. Food and Drug Administration and is not referenced in the U.S. Department of Health and Human Service, it is prescribed "off label" by some clinicians in the United States, and it remains a popular option in other countries.

With the development of its extended-release formulation of nevirapine, Viramune XR (400mg nevirapine), manufacturer Boehringer Ingelheim (BI) appears to have its sight set on once-daily approval of the drug. In Vienna, Anne-Marie Quinson, MD, of BI and her colleagues presented the long-awaited results from the VERxVE study evaluating the safety and efficacy of this investigational compound.

The study randomized 508 treatment-naive individuals to the standard Viramune group (200 mg taken twice daily) and 505 to the Viramune XR group, with patients in both groups also receiving Truvada (tenofovir plus emtricitabine). The average age of participants entering the study was 38, and about 85 percent of the study volunteers were men. About 250 patients were enrolled in the study through European research centers; about 150 were enrolled in the United States; and the remaining patients were enrolled through sites in Latin America or Africa.

Viral loads at study entry were about 50,000 copies, and CD4 counts averaged 228 cells.

About 82 percent of those enrolled in the study completed 48 weeks of follow-up, with no significant differences between the two groups. Adverse events (occurring in 7.3 percent) and lack of efficacy (documented in 4.9 percent) were the most common reasons for study discontinuation.

Of note, all patients enrolled in the study began treatment with a 14-day lead-in period in which they took one 200 mg tablet of standard Viramune once a day, before starting full dosing—a common practice to reduce the risk of Viramune toxicity upon commencing treatment.

After 48 weeks, a viral load below 50 copies was maintained in 76 percent of patients in the standard Viramune group, compared with 81 percent of patients in the Viramune XR. Given that the difference between the two groups was within a pre-specified 10 percent margin of each other—with a 4.92 percent difference in favor of Viramune XR—Viramune XR was concluded to be "non-inferior" to standard Viramune.

In patients with pre-treatment viral loads greater than 100,000 copies, the response rate was 73 percent in the Viramune XR group, compared with 71 in the standard Viramune group. Among patients with pre-treatment viral loads at or below 100,000 copies, the response rate was 79 percent in the standard Viramune group, compared with 86 percent in the Viramune XR group.

The most common adverse events in the Viramune XR group were nasopharyngitis—inflammation of the nasal passages—diarrhea, upper respiratory tract infection, rash and headache. No new or unexpected safety concerns emerged in the standard Viramune group.

The rate of discontinuations due to adverse events in the Viramune XR group was 6.3 percent, compared with 8.9 percent in the standard Viramune group.

The rate of symptomatic liver problems was 1.6 percent in Viramune XR–treated patients, compared with 2.8 percent of those taking standard Viramune.

Rashes developed in about 8.5 percent of patients in all patients, with no discernable differences between the two groups.

Three cases of Stevens-Johnson syndrome (SJS)—a potentially serious skin-related adverse event—occurred during the 14-day lead-in phase of dosing; an additional two cases were reported in the standard Viramune group following lead-in dosing. While there were no cases of SJS in the Viramune XR group, Boehringer Ingelheim warns that this does not mean it can't happen.

Though cholesterol levels increased in both Viramune groups, increases in "good" HDL increases were more pronounced in he Viramune XR group, leading to a more favorable cholesterol ratio.

VERxVE researchers also conducted a sub-study involving about 25 patients enrolled in each study group to compare drug levels in the body. According to Quinson, nevirapine blood levels using Viramune XR remained consistent over a 24-hour period, with both groups having similar trough levels—the concentration of drug in the bloodstream immediately before a subsequent dose is given.

In conclusion, with its non-inferior efficacy and similar safety/tolerability profile to standard Viramune, Quinson's team concluded that Viramune XR may ultimately provide patients with a more convenient treatment regimen. BI is currently working with regulatory authorities to make Viramune XR available.

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