Intracranial Hemorrhage Risk Prompts Changes to Aptivus Label

**Reports of fatal and nonfatal intracranial hemorrhage among HIV-infected patients taking Aptivus (tipranavir) in combination antiretroviral therapy have prompted the manufacturer to issue new safety information.**

Boehringer Ingelheim Pharmaceuticals Inc. has identified 14 reports of intracranial hemorrhage, including 8 fatalities, in 6,840 HIV-infected individuals receiving Aptivus capsules coadministered with ritonavir (Norvir) (500 mg/200 mg twice daily).

Many of these patients who developed intracranial hemorrhage had other medical conditions—CNS lesions, head trauma, recent neurosurgery, coagulopathy, hypertension, or alcohol abuse—or were receiving concomitant medications, including anticoagulants and antiplatelet agents, that may have caused or contributed to these events.

Several sections of the label have been revised to reflect concerns about using the drug in patients at increased risk of bleeding. No pattern of abnormal coagulation parameters has been identified in patients receiving Aptivus in general or preceding development of intracranial hemorrhage. For this reason, routine measurement of coagulation parameters is not currently indicated for the management of patients taking the drug.

Aptivus/ritonavir therapy should be used cautiously in patients who may be at risk for increased bleeding from trauma, surgery, or medical conditions, or who are taking other drugs known to increase the risk of bleeding. Of note, patients with advanced HIV disease/AIDS have been observed to have an increased risk of intracranial hemorrhage. Investigations are ongoing to determine the role of Aptivus in the development of intracranial hemorrhage.

For more information or to report adverse reactions, Boehringer Ingelheim Pharmaceuticals can be contacted by calling 800-542-6257 (option 4). Adverse reactions can also be reported to the Food and Drug Administration’s MedWatch program by calling 800-332-1088.

—Kerri Wachter

Older HIV Patients More Likely To Comply With Treatment

**BY FRAN LOWRY**

**Toronto** — With age comes enhanced adherence to HIV therapy, according to a study presented at the 16th International AIDS Conference.

Michael J. Silverberg, Ph.D., of Kaiser Permanente’s Division of Research, Oakland, Calif., and his associates took a prospective look at about 9,000 HIV-positive patients aged at least 50 years. All were in the Kaiser Permanente Northern California health plan for the 6 months prior to antiretroviral therapy.

They found that subjects over age 50 were more adherent to highly active antiretroviral therapy (HAART)—a cocktail of a protease inhibitor plus two reverse transcriptase inhibitors—than were younger patients.

As a result, they were 15% more likely to reach undetectable levels of HIV infection and had higher CD4 counts.

**Silverberg**

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**Dr. Silverberg**

Laboratory abnormalities frequently seen after initiation of HAART in older individuals included hyperglycemia, abnormal bilirubin, neutropenia, ALT and AST elevations, and elevated creatinine. Dr. Silverberg said.

“Because of these abnormalities, we feel that older patients need particularly close monitoring at the beginning of a HAART regimen,” Dr. Silverberg said. “However, they do quite well. I guess with age, people become more disciplined with their treatment,” he added.

**Four Drugs No Better Than Three for Initial HIV Tx**

**By Fran Lowry**

**Toronto** — Adding a fourth drug to a standard three-drug regimen in the initial treatment of HIV-infected subjects has not added to virologic suppression, according to reports presented at the 16th International AIDS Conference.

“The high rates of virologic suppression achieved in this study support current guidelines that recommend two nucleosides plus efavirenz among preferred regimens for the initial treatment of HIV-1 infection. Adding abacavir as a fourth drug to the standard initial three-drug regimen did not change toxicity or adherence but provided no additional benefit,” said Dr. Roy M. Gulick of Weill Cornell Medical College, New York.

The standard three-drug regimen is effective for most individuals with HIV, but some researchers have hypothesized that if the initial three-drug regimen did not change the viral load at 3 years, as were the CD4 cell counts and incidence of adverse events. The study participants did well, with more than 80% reducing their HIV RNA levels to less than 50 copies/mL at 3 years, he noted.

“Our study affirms that the three-drug regimen we use to treat HIV infection today is very effective for most people, and adding a fourth drug is of no benefit in terms of decreasing viral load levels or increasing T cells,” Dr. Gulick said. He added in an interview:

**Dr. Gulick**

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**Four Drugs No Better Than Three for Initial HIV Tx**

**BY FRAN LOWRY**

**Toronto** — A large, randomized comparison of three standard regimens for initial treatment of HIV has shown that all are safe and effective, but the three-drug regimen of efavirenz plus two nucleosides was significantly better at reducing HIV viral load, investigators said at the 16th International AIDS Conference.

The regimens for first-line therapy of HIV that are currently recommended by the Department of Health and Human Services are the protease inhibitor lopinavir and the nucleoside reverse transcriptase inhibitor efavirenz, each given with two nucleoside reverse transcriptase inhibitors.

However, these regimens have not been compared in adequately powered, randomized clinical trials. Nor has the nucleoside-sparing regimen of efavirenz plus lopinavir, Dr. Sharon A. Ruddler, of the University of Pittsburgh, and his associates took a prospective look at about 1,600 naive subjects with HIV RNA greater than 2,000 copies/mL and any CD4 cell count. Participants were randomized equally in one of three arms: lopinavir soft gel capsules plus two nucleosides, efavirenz plus two nucleosides, and lopinavir soft gel capsules plus efavirenz.

With a median follow-up of 112 weeks, the time to virologic failure was significantly shorter in the lopinavir plus two nucleosides arm, compared with the efavirenz plus two nucleosides arm. At week 96, the proportion of subjects without virologic failure was 78% in the efavirenz plus two nucleosides arm, 74% for lopinavir plus efavirenz, and 67% for lopinavir plus two nucleosides, Dr. Ruddler reported.

“Our findings suggest that the efavirenz plus two nucleosides was the best of the three approaches as initial therapy, even in patients with relatively advanced HIV disease,” she said.

“The main message from this study is that it is an incremental step toward understanding the most useful regimens to be used for initial therapy in HIV-infected individuals,” Dr. Ruddler said in an interview. ‘All of the three regimens were effective, with significant increases in CD4 cell counts and the vast majority of individuals having undetectable viral loads, regardless of which regimen was initiated.”

ACTG 5142 is the first study to look at these three standard-care regimens in naive individuals randomized upfront, and the data are important for how we actually tease out a lopinavir-based regimen compared to an efavirenz-based regimen,” said Dr. Scott M. Hammer, professor of medicine at Columbia University, New York, and an ACTG investigator.

**Efavirenz-Based Treatment Better at Reducing Viral Load**

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