FDA Approves First-in-Class Integrase Inhibitor for Treatment-Resistant HIV-1

October 15, 2007
By Peggy Peck [1]

WHITEHOUSE STATION, N.J. -- The FDA has approved raltegravir (Isentress) as part of a combination regimen for treatment for multi-resistant HIV-1 infection in adults, according to an announcement from Merck.

The company said the approval emerged from analyses of plasma HIV-1 RNA levels up through 24 weeks in two controlled studies of raltegravir (400 mg tablet bid) plus optimized background therapy. It is the first drug approved in a new class of antiretroviral agents called integrase inhibitors.

The drug works by inhibiting the insertion of HIV DNA into human DNA via the integrase enzyme, which blocks the ability of the virus to replicate and infect new cells.

The studies were conducted in clinically advanced patients with virus resistant to agents three antiretroviral classes (nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and protease inhibitors). In those studies, patients randomized to raltegravir plus optimized background therapy achieved significant reductions in HIV RNA viral load and increased CD4 cell counts compared with placebo plus optimal therapy.

The company said, however, that the safety and efficacy of raltegravir has not been established in treatment-naive patients, nor are there data demonstrating an effect on clinical progression of HIV-1 infection.

Joseph J. Eron, Jr., M.D., of the University of North Carolina in Chapel Hill, who was an investigator for the company-sponsored trials, called the approval a "significant milestone in the history of HIV/AIDS therapy because we now have a drug that's potent against another key enzyme essential for viral replication."

Dr. Eron said, however, that it was important to recognize that the drug should not be used as monotherapy, but must always be used in combination with other active agents.

The most commonly reported adverse experiences were diarrhea, nausea, headache, and fever.

Additionally, creatine kinase elevations were observed in patients who received raltegravir and both myopathy and rhabdomyolysis have been reported, although the relationship of raltegravir to these events is not known. The company said the drug should be used with caution in patients at increased risk of myopathy or rhabdomyolysis, such as patients receiving concomitant medication known to cause these conditions.

(See: ICAAC: Integrase Inhibitor Effective for HIV Patients with Multi-drug Resistant Disease)

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