Novel Drugs Show High Efficacy for Resistant HIV

BY TIMOTHY F. KIRN
Sacramento Bureau

LOS ANGELES — Two novel HIV medications produced striking improvement in AIDS patients otherwise failing standard therapy, according to four separate studies presented at a conference on retroviruses and opportunistic infections.

"The results here are as exciting as the development of HAART [highly active antiretroviral therapy] for treatment-experienced patients," said Dr. John W. Mellors, chief of infectious diseases at the University of Pittsburgh, commenting on the studies at a press briefing.

Each drug reduced viral loads to fewer than 400 copies/mL in 60%-80% of study patients, who already had resistance to currently available drugs.

"This is really a remarkable development in the field," added Dr. Mellors, who is also codirector of the center for viral diseases at the University of Pittsburgh.

One of the drugs, Pfizer Inc.'s maraviroc, is an antagonist to the CCR5 coreceptor used by HIV to enter CD4-positive T cells. The other drug, Merck & Co.'s raltegravir, is an integrase inhibitor, which blocks viral genes from being incorporated into the host cell genome where they can be activated.

In one trial of maraviroc conducted in Europe, Australia, and North America, the drug reduced HIV RNA levels to below 400 copies/mL at 24 weeks in 55% of 182 triple-class–experienced patients who took the drug (150 or 300 mg) once daily in addition to their optimized, standard therapy. The drug reduced viral loads below that level in 61% of 191 patients who took the drug twice daily, reported Dr. Howard Mayer, executive director for global research and development at Pfizer.

That compared with only 23% of 91 placebo-treated patients whose viral loads dropped below that level, he said at the conference, sponsored by the Foundation for Retrovirology and Human Health.

The dosage that the patients received in the trial—either 150 mg or 300 mg—depended on what drugs were in their optimized background therapy during the trial. Patients whose background treatment regimen included a protease inhibitor or delavirdine received the lower dose.

In a second trial conducted only in the United States and Canada, the results were almost the same. Of the 232 patients who took the drug once daily, 55% had viral levels that dropped below 400 copies/mL, as did those of 60% of 235 patients who took the drug twice daily. That compared with 31% of 118 placebo-treated patients.

For treatment of patients with drug-resistant HIV, 'this is really a remarkable development in the field.'

DR. MELLORS

Raltegravir (400 mg twice daily) decreased the HIV RNA level to less than 400 copies/mL in 77% of 232 patients with triple-class–resistant virus on optimized therapy, versus 41% of 118 placebo-treated patients, at 16 weeks, reported Dr. David Cooper, head of the immunology, HIV, and infectious diseases clinical services unit at St. Vincent's Hospital, Sydney.

In a second study, those percentages were 77% and 43%, respectively.

Maraviroc produced viral RNA loads of fewer than 50 copies/mL—considered an undetectable viral load—in 40%-48% of treated patients in its two studies, compared with 21% and 24% of placebo-treated patients.

Raltegravir produced viral loads of fewer than 50 copies/mL in 61% and 62% of treated patients, versus 33% and 36% of placebo patients.

Mean CD4 T-cell levels increased to a greater degree in treated patients for both drugs, and both drugs had low discontinuation rates that were comparable with discontinuations in placebo patients.

According to Pfizer, maraviroc is receiving accelerated review by the U.S. Food and Drug Administration and in Europe.

Merck is providing expanded access to raltegravir for patients unable to participate in a clinical trial.

If approved, the drugs should find ready use. It is estimated that 5%-15% of new infections are infections with virus that already has some resistance to available drugs, said Dr. Mellors, who called the results a "milestone" in HIV therapy. ■