Better Strategies Need Funds in Fight Against AIDS

BY BETSY BATES
Los Angeles Bureau

LOS ANGELES — The number of Americans diagnosed with AIDS is now approaching the 1 million mark, with more than a half-million deaths since the epidemic began and 17,000 more people dying of the disease each year, Dr. Harold Jaffe said at the 14th Conference on Retroviruses and Opportunistic Infections.

That mortality—58 per million—is "twice as high as any country in the European Union and 10 times as high as in the United Kingdom," said Dr. Jaffe, former director of HIV prevention for the Centers for Disease Control and Prevention and currently head of the department of public health at Oxford University, England.

A troubling jump in incidence in 2005, the latest year for which data are available, compounded by signs of risky behavioral trends in gay men, points to the critical need for community leadership, personal responsibility, and support of preventive efforts proven to work, he said.

"The need for treatment is critical, but I agree with my colleague [WHO director of HIV/AIDS] Dr. Kevin de Kock that we are not going to be able to treat our way out of this epidemic," added Dr. Jaffe, who singled out federal funding for abstinence-only education as an example of a strategy based on beliefs rather than science.

A "very comprehensive" study in press in the Cochrane Review, for example, reviewed eight published randomized controlled trials of abstinence-only programs, compared with standard sex education or safe-sex programs, involving 13,191 American youths. With a median follow-up of 12 months, none of the abstinence-only programs demonstrated a significant decline in self-reported sexual activity or any biological outcome such as pregnancy or diagnosis with a sexually transmitted disease (STD), compared with the other approaches, said Dr. Jaffe at the conference, sponsored by the Foundation for Retrovirology and Human Health.

A University of Pennsylvania study of 662 African American children (median age, 12 years) did show significantly less sexual activity among those receiving abstinence-only education, compared with those exposed to other interventions; even so, nearly a third of the virgins in the abstinence-only group became sexually active over the course of the 2-year study.

By contrast, condom promotion has been shown to be "highly efficacious" in preventing HIV transmission, and needle- and syringe-exchange programs, which demonstrate at least modest evidence of reducing intermediate-level activities with the capacity to spread HIV, as more effective approaches.

President Bush's proposed 2007 budget includes $204 million in support of abstinence-only education, while "no administration, Democrat or Republican, has ever put any [federal] money whatsoever into needle-exchange programs in this country, in contrast to many other countries, including the U.K.," Dr. Jaffe said.

Purely behavioral interventions, primarily skill-building sessions aimed at reducing risky activities among high-risk individuals, are highly significantly efficacious in reducing unprotected sex and acquiring STDs, he said.

Finally, HIV testing by itself is a profound risk-reducing strategy, because individuals who learn they have been exposed to the virus sharply reduce behaviors that could lead to transmission to others, he noted.

Some indicators suggest that resources must be quickly marshaled to stem a rising tide of cases, especially among men who have sex with men and among African Americans and other ethnic minorities.

"We are seeing behavior trends in gay men in the United States and Western Europe that are similar to trends in the late 70s, years just before tens of thousands of young men were about to lose their lives," he said.

He urged activists and community leaders to "step forward" and policy makers "to use science rather than moral judgment, religious beliefs, or wishful thinking to guide our strategies." ■

Novel HIV Drugs Show High Efficacy in Resistant Disease

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.

The results are as exciting as the development of HAART for treatment-experienced patients.

DR. MELLORS

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, said 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 a 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, said 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, which was sponsored by the Foundation for Retrovirology and Human Health.

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.

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.

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 currently estimated that 5%-15% of new infections are infections with virus that already has some resistance to currently available drugs, said Dr. Mellors, who called the results a "milestone" in HIV therapy. ■

Low CD4 Counts Tied to Nonopportunistic Disease Risks

BY BETSY BATES
Los Angeles Bureau

LOS ANGELES — The risk of nonopportunistic diseases in HIV-infected patients increases as CD4 counts fall, and the impact of such diseases overshadows that of opportunistic diseases at CD4 counts above 200 cells/mcL, said Dr. Jason Baker of the University of Minnesota in Minneapolis.

The discovery that rates of nonopportunistic diseases vary according to CD4 counts "starts to build a case that people aren't just … living longer and … dying of other causes," Dr. Baker said at a press conference following his presentation at the 14th Conference on Retroviruses and Opportunistic Infections.

Rates of liver, renal, and cardiovascular diseases, as well as of non–HIV-related cancers, were all associated with CD4 counts in a group of 1,397 patients followed for at least 5 years after enrollment in a study sponsored by the National Institutes of Health.

Dr. Baker and his associates randomly assigned ART-naive patients to one of three drug regimens and carefully monitored all fatal and nonfatal opportunistic and nonopportunistic events.

Over the 5-year follow-up, there were 266 opportunistic disease events with 89 related deaths and 166 nonopportunistic disease events with 25 deaths.

Nonopportunistic diseases seen in the cohort included cirrhosis and grade 4 transaminitis; myocardial infarctions, strokes, and coronary artery disease requiring intervention; renal insufficiency and end-stage renal disease; and 32 malignancies other than non-Hodgkin's lymphoma or Kaposi's sarcoma, including five cases each of anal, lung, and skin cancers.

Liver disease disproportionately included grade 4 elevated liver enzymes, which may be related to medications. Whether or not this diagnosis was included in the analysis, however, CD4 counts were related to disease events. Both opportunistic and nonopportunistic events were less likely in patients with higher CD4 counts.

"The decline was steeper for opportunistic disease events, but nonopportunistic disease became at least as significant if not more so at higher CD4 levels," Dr. Baker said at the conference, sponsored by the Foundation for Retrovirology and Human Health.

Above CD4 counts of 200 cells/mcL, mortality and morbidity were higher for nonopportunistic than opportunistic disease, he said.

The univariate hazard ratios for the difference in risk for an incremental increase of 100 cells/mcL in the CD4 count was 0.49 for opportunistic disease and 0.78 for nonopportunistic disease, and remained powerful (0.57 and 0.84, respectively) even after adjustment for age, sex, race, prior AIDS, hepatitis B and C, baseline CD4 and RNA viral load, and latest RNA viral load, Dr. Backer said. ■