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Upfront

Kristen Romanowski and Daniel Bond

More women and teens needed for HIV vaccine clinical trials

More women and adolescents are needed to participate in HIV vaccine clinical trials, say 40 international experts brought together by the World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) to discuss gender, age, and race in HIV vaccine research and clinical trials.

At a late August meeting in Lausanne, Switzerland, experts agreed that women, particularly girls, are often excluded or unlikely to participate in HIV vaccine clinical trials, even though they would be major beneficiaries of a future vaccine for the virus that disproportionately affects women and girls. Studies show that, when exposed to the virus, women are at least twice as likely to become infected with HIV as are males.

“Clinical trial enrollment needs to be more inclusive, so the benefits of research are more fairly distributed,” meeting co-Chair Ruth Macklin said in a WHO press release.

The WHO-UNAIDS HIV Vaccine Initiative aims to develop licensed and effective vaccines that are accessible by all, regardless of gender, age, socioeconomic status, race, ethnicity, or country. The initiative stipulates that vulnerable groups, particularly women and girls, must benefit from an HIV vaccine.

Girls and young women aged 15 to 24 account for 62 percent of the young people living with HIV or AIDS in developing countries, and, in parts of sub-Saharan Africa, are up to six times more likely to be infected than their male peers. Youth in general are also at high risk for contracting the virus, with about half of the new HIV infections in the developing world occurring among 15- to 24-year-olds.

Despite these statistics, women and youth are not participating in clinical trials at the same level as adult men for many reasons, including lack of empowerment and education, social isolation, discrimination, cultural stigma, pregnancy, and issues of confidentiality and informed consent, according to the WHO.

Because vaccines for several infectious diseases have shown different levels of effectiveness among different gender, age, racial, and ethnic groups, a potential HIV vaccine must be tested in varied populations, experts at the meeting agreed. For example, a clinical trial from 1998 to 2003 of VaxGen's AIDSVAX found that although the vaccine was not effective overall, non-whites and women possibly had a degree of protection, a finding which calls for further study.

The number of AIDS vaccine candidates in small-scale human trials has doubled since 2000, and 30 new candidates are now being tested in clinical trials in 19 countries. A safe, effective, and affordable HIV vaccine would be a momentous achievement in the battle against the AIDS epidemic, which continues to infect five million adults and children and kill three million people each year. ***—KR***

Vioxx withdrawal shakes pharmaceutical industry

One of the most widely prescribed arthritis and acute pain medications in the world has been pulled from the market, causing long-term implications for both the maker and users of the drug, as well as for the regulatory process used to guarantee drug safety. In late September, drug maker Merck set off a storm of public controversy when it announced a voluntary withdrawal of Vioxx from the worldwide market.

The withdrawal comes in response to Merck's own research, which linked the drug to an increased risk of coronary disease. Ironically, Merck's study was designed to discover if Vioxx could help prevent the recurrence of potentially cancerous polyps, a trait which could have significantly increased Vioxx's presence in the market. Instead, researchers discovered that, after 18 months, participants taking Vioxx regularly had double the risk of heart attack or stroke as those on a placebo. Prior to Merck's recall, numerous studies had suggested that Vioxx might be linked to high blood pressure and heart disease in chronic users.

"We are taking this action because we believe it best serves the interests of patients," Merck CEO Raymond V. Gilmartin said in a press release. Gilmartin stopped short of acknowledging suggestions that the drug could be a killer, maintaining that "it would have been possible to continue to market Vioxx with labeling that would incorporate these new data."

The withdrawal has led some to charge the Food and Drug Administration (FDA) with negligence for approving the drug in 1999. Thomas Moore, a health policy analyst for George Washington University, told Reuters that, in the face "of mounting evidence over five years that this drug had cardiovascular risks, [the FDA] settled for almost a minimal amount of action, a small change in the product labeling." The labeling change was not enough, Moore said. "The result of this is, literally, millions of people wake up one morning and discover they were taking a drug that did more harm than good," he said.

These developments have cast a shadow across all COX-2 inhibitors, the drug family to which Vioxx belongs. Since their introduction to the market, COX-2 inhibitors have been touted by many as "safer" pain relievers because, unlike ibuprofen or naproxen, they block inflammation while also protecting the stomach lining, meaning fewer users suffer from stomach irritation.

Pfizer, the makers of Celebrex, a COX-2 inhibitor prescribed widely as an alternative to Vioxx, recently told the Wall Street Journal that the company has been monitoring three studies on cardiovascular side effects and has found "none of the safety problems Merck found with Vioxx." The current Celebrex label states that cardiovascular side effects are "possible, but uncommon."

The withdrawal has also resulted in a spate of class action lawsuits against Merck. In Canada, one suit targets Merck and its Canadian subsidiaries, and another charges that Canada's attorney general and health minister were complicit in Merck's failure to heed early warnings about the risks associated with Vioxx.

In Illinois, a class action suit representing an estimated 300,000 state residents has been filed and awaits certification from local courts. Michael Moirano, one of the lawyers representing Illinois users, released a statement claiming that Merck "intentionally tried to downplay the findings" until the evidence against the drug "was so overwhelming they had no choice."

Despite major setbacks, including financial losses, Merck plans to continue clinical tests for Arcoxia, a new medication being developed to replace Vioxx. ***—DB***

Mood disorders and their treatments may have oral side effects

Patients who suffer from mood disorders like major depression and bipolar disorders need special oral health care, according to the September/October 2004 issue of *General Dentistry*.

Because depressed patients often lose interest in oral hygiene, and patients with mania can cause tooth abrasion and gingival injury by brushing and flossing excessively, oral health care providers must be able to recognize the signs of various mood disorders and refer patients for evaluation and treatment.

Patients receiving treatment for mood disorders must also be carefully monitored. “An aggressive, effective oral hygiene program is important for patients with mood disorders because many of the drugs used to treat these disorders produce xerostomia, which increases the risk for dental caries, periodontal disease, and fungal infections,” author James W. Little, DMD, writes.

To combat the side effects of antidepressants and mood-stabilizing drugs, oral health care providers should advocate preventive measures like artificial salivary products, antiseptic mouthwash, and daily fluoride rinses. They must also be careful to avoid drug interactions when giving dental treatment.

Major depression affects up to 37 percent of American adults and is more common among women than among men. In adolescence, girls are twice as likely as boys to be diagnosed with depression. ***—KR***

Lupus sufferers find relief in cancer drug

A drug now used to treat a form of cancer may be a blessing to those who suffer from lupus, according to research published in the August issue of *Arthritis and Rheumatism*. The results of a 12-month clinical study conducted by physicians at the University of Rochester Medical Center show that rituximab, a drug used to treat lymphoma, significantly improved the health of 11 of 17 lupus patients injected with the drug. Several patients were able to go off or reduce their traditional lupus medications.

Lupus is a chronic disease that causes the body’s immune system to lose the ability to tell the difference between foreign substances and its own cells and tissue. The immune system then attacks the body’s own tissue and major organs, causing a wide range of symptoms, the most common of which include achy and swollen joints, frequent fevers, extreme fatigue, and skin rashes.

Four out of 10 patients with lupus take six medications or more to control their symptoms. Commonly prescribed medications include non-steroidal anti-inflammatory drugs, acetaminophen, cortcosteroids, antimalarials, and immunomodulating drugs.

Although lupus can affect any organ, including the heart, brain, lungs, and kidney, it is not necessarily life-threatening. According to the Web site of the Lupus Foundation of America, “the idea that lupus is generally a fatal disease is one of the gravest misconceptions about the illness.” The Foundation estimates that approximately 1.5 million American suffer from some form of the disease, 90 percent of whom are women. Lupus is also two to three times more common among African Americans, Hispanics, Asians, and Native Americans.

In lupus patients, B cells are found in the wrong proportions in blood and tissue, and they make antibodies that mistakenly attack the body itself. Because lupus involves the same immune B cells as lymphoma, the University of Rochester researchers suspected that rituximab would also be successful at treating lupus. The 11 patients who showed the most improvement in this study, in fact, also showed significant drops in their B cells.

Besides improvements in health, patients in the study experienced few side effects. Because the cancer drug precisely targets B cells, aiming to lower their numbers, rituximab carries fewer side effects than current lupus treatments, which can leave patients vulnerable to infection, heart disease, glaucoma, depression, thinning bones, weak muscles, and weight gain.

Researchers say that rituximab is the first new, targeted therapy to be discovered in a long time, and the team is now helping to design a larger study with multiple sites around the nation. ***—KR***