Looking Back, Moving Forward: The Year in Treatment News

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Now more than 25 years since the 1983 discovery of HIV as the cause of AIDS, research continues at a steady clip in pursuit of sound prevention strategies, better treatments and—with a little bit of luck—a cure. While 2008 wasn't exactly a year of earth-shattering discoveries, there were advances, setbacks and a few telltale hints of interesting things to come in 2009.

What follows is a review—including updated insight from some leading HIV activists— of the top 10 treatment research developments that made us sit up straight in 2008. Have additional news items to add to the list? New observations or experiences of your own to share? Let us know by posting a comment at the end of this article.

New Numbers

After months of speculation, the U.S. Centers for Disease Control and Prevention (CDC) released new data in early August confirming thousands more annual HIV cases than was previously believed. The numbers—56,300 new HIV infections in 2006, compared with the 40,000 estimate—sent prevention and treatment activists scurrying for answers and solutions to the instantly-ballooned U.S. epidemic.

The CDC was quick to point out that the number of new infections has remained fairly stable during the past decade, albeit many more than was originally thought. Activists, however, still had difficulty stomaching the new estimate. "The incidence figures, labeled by the CDC as evidence of a 'stable' epidemic, actually reveal an unabated rise in the number of new infections among gay men, particularly young gay men of color," explains Julie Davids, senior consultant of the prevention-focused Community HIV/AIDS Mobilization Project (CHAMP) in New York and Providence.

“It’s clear that we need a national AIDS strategy that spans treatment and prevention, and that specifically addresses the urgent need for prevention innovation,” Davids adds. “This must include an investment in research as well as measures that challenge and change the root causes of HIV—such as homophobia and mass imprisonment—that fuel marginalization.”

When to Start

“From colds to cancer, it is almost always better to treat a disease earlier rather than later; HIV is no exception,” says Washington, DC-based biomedical journalist Bob Roehr, referring to three recent studies indicating that antiretroviral (ARV) therapy should be started sooner than later. A 2,000-patient Spanish study, the 1,400-patient FIRST trial and the U.S. and Canadian NA-ACCORD study, all reported in 2008, suggest HIV-positive people initiating ARV treatment with CD4s above 350 face a reduced risk of AIDS- and non-AIDS-related health problems and deaths compared with those starting with CD4s below 350—the current green light for commencing therapy.

Arguments against early therapy, many contend, are also losing ground. “The hang-up with HIV has been side effects, including nausea, lipodystrophy and damage to cell mitochondria,” Roehr says. “New treatments are more powerful at suppressing the virus and have fewer side effects, so it is no surprise that the trend is to starting treatment earlier.”

While many experts agree that it’s only a matter of time before the official Department of Health and Human Services (DHHS) HIV treatment guidelines are amended to promote early treatment, Roehr argues that individualized care—based on a patient’s specific risk factors, needs and limitations—must take precedence over cookie-cutter approaches to care. “Treatment HIV is not a static formula,” he says. “It remains a medical art; it is a dance between doctor and patient where a good partnership is crucial.”

Introducing Intelence

The year began with excellent news when the FDA approved Tibotec’s twice-daily Intelence (etravirine). Not only was it the first new non-nucleoside reverse transcriptase inhibitor (NNRTI) in 10 years, but studies also confirmed its effectiveness for HIV-positive patients with resistance to first-generation NNRTIs, such as Viramune (nevirapine) and Sustiva (efavirenz). Study results also emerged suggesting that Intelence may be potent enough, used once a day, for those starting treatment for the first time.

“Intelence comes with the baggage of hope,” says Bob Huff, editorial and antiretroviral project director of the New York-based Treatment Action Group. “Intelence made its mark by helping people with long and troubled treatment histories achieve viral suppression for perhaps the first time in their lives.”

The arrival of Intelence has also opened up promising possibilities. One potential option to explore in future studies, explains Huff, is using nucleoside analogue-sparing regimens for first-line therapy, “perhaps combining Intelence with unboosted Reyataz for a clean and durable twice-daily combination.”

“For all the promise,” Huff adds, “Intelence is still young and relatively fragile when it comes to combating resistance. In 2009, results from dozens of studies examining the drug’s potential will begin to reveal whether these hopes are more than wishes.”

Epzicom Woes

It was a frustrating year for Epzicom, GlaxoSmithKline’s two-in-one tablet containing the nucleoside reverse transcriptase inhibitors abacavir and lamivudine. The D:A:D study and SMART trial linked abacavir to a higher risk of heart attacks, whereas the AIDS Clinical Trials Group study 5202 (ACTG 5202) reported a higher rate of treatment failure among Epzicom-treated patients starting therapy with viral loads above 100,000 copies. These findings not only resulted in the DHHS demotion of Epzicom as a preferred treatment option for first-time treatment takers, but also left those already using the drug—many without any signs of trouble—scrambling to determine whether a switch was necessary.

While GSK and independent research teams continue to make neither heads nor tails of the data, experts stress that Epzicom is an effective treatment option for many people living with HIV. “The need for the Epzicom option could outweigh potential risks, as with any drug combination and medical history and clinical status,” says Ken Fornataro, executive director of the AIDS Treatment Data Network in New York. “Obviously a high viral load is going to put pressure on a treating physician to avoid using it in that case, but it’s all about what options exist and what it is combined with. There could be competing concerns of potential side effects with another recommended combination. This is one of those cases that reinforce the need for patients to discuss their past, present and future treatment options with their doctors.”

Pipeline Problems

Activist circles were abuzz with ominous speculation regarding the state of HIV treatment research and a dearth of promising compounds in the pipeline after receiving word that pharmaceuticals giant Roche had terminated its in-house HIV research. “The search for better AIDS meds seems to have paused after a flurry of new drug approvals in the past year and a half,” explains TAG’s Huff. “Some companies say they’ve tried but haven’t been able to top their current best sellers. Others have gained approval for innovative new HIV drugs, only to see them languish in the marketplace.”

Some argue that the Roche’s decision isn’t necessarily a sign of trouble ahead. “More isn’t necessarily better; better is better,” says Roehr, the biomedical journalist. “Scientifically, it has become very difficult to make better HIV drugs because those now available use so many different mechanisms of action and have such good tolerability and durability. The rough economy reinforces this scientific message.”

Huff, however, says there is much room for improvement with ARVs. “Too many HIV physicians appear content to ‘set it and forget it’ with one pill once a day,” he points out. “Such complacency is misguided and may be misleading the pharmaceutical industry to believe that there is no urgency to finding better HIV drugs. We may be in a trough between new drug approvals, but the

need for AIDS treatment is not over."

Undetectable = Uninfectious?

In January, the Swiss Federal Commission for HIV issued a surprising statement: People living with HIV with undetectable viral loads and no other sexually transmitted infections (STIs) are not "sexually infectious." This claim, however, has since been the subject of much debate.

Few experts deny data confirming a low risk of HIV transmission by positive people with low viral loads and, as a result, that ARV therapy is a key player in HIV prevention efforts. What irks some, however, is the black-and-white tenor of the Swiss Statement, especially when it is based on a handful of studies that only enrolled HIV-discordant heterosexual couples in sexually monogamous relationships.

"We know that oral sex has, at best, a very low risk of HIV transmission but that it will be very difficult or impossible to prove that it is no risk," says CHAMP's Davids. "Similarly, there are major methodological challenges to proving the veracity of elimination of transmission risk among those who are undetectable and STD-free. The Swiss Statement is a challenge to prevention experts who need to provide information that is not only accurate to the best of their knowledge, but also offers practical tools for decision making across the lifespan of people living with HIV."

Staph Troubles

While not considered an AIDS-defining illness, drug-resistant staph infections have become a serious concern among HIV-positive people and the care providers who treat them. A handful of 2008 studies confirmed that methicillin-resistant Staphylococcus aureus (MRSA) is not only more likely to occur in people living with HIV compared with their negative counterparts but also more likely to recur after treatment.

"We've started seeing MRSA more and more frequently in the last few years, and unfortunately, it's on the rise and not going away any time soon," explains Chicago-based Jeff Berry, editor of Positively Aware magazine. "Studies show that many of these infections are sexually transmitted and that those with a lower CD4 count are more at risk. Being on HIV treatment reduces your risk, but it's still a very real threat, and some of the MRSA treatments interact with certain HIV meds."

Berry cautions that MRSA can be disfiguring and easily spread, "so if you think you may have it, seek treatment immediately." He also spells out a few prevention strategies: "Use a harm-reduction approach by limiting your sexual partners, not sharing needles, using clean towels at home and at the gym, using good hygiene, and using a condom—although even that is no guarantee, since it is transmitted via skin-to-skin contact."

Transplanting Hope

Not every remarkable HIV treatment discovery makes the front page of the morning papers. Take, for example, the apparent eradication of HIV from an HIV-positive patient in Berlin undergoing a bone marrow transplant to treat his leukemia, first reported at the 15th annual Conference on

Retroviruses and Opportunistic Infections (CROI) in Boston earlier this year. Only recently has the report made headlines, renewing the biggest question of them all: Can HIV be cured?

The man's transplant team used stem cells from a donor with a rare genetic mutation that prevented his CD4 cells from producing CCR5 receptors and, thus, rendered him virtually immune to HIV. Even if the patient turns out to have beat back HIV permanently—further analysis of his blood and tissue samples is still needed—it is unlikely that stem cell transplants are going to become a routine treatment. For starters, patients must first undergo whole-body radiation or high-dose chemotherapy to make space for the transplanted cells, both of which come with a high risk of serious side effects and death.

Will this intriguing case pave the way for similar—yet kinder and gentler—curative approaches, such as therapies to "turn off" genes responsible for producing CCR5 on CD4 cells? "It may be evident that reducing HIV reservoirs and enhancing the resistance of CD4 cells can lead to a functional cure," says Richard Jefferys, coordinator of the Treatment Action Group's Michael Palm Basic Science, Vaccines and Prevention Project. "But scientists need to figure out how to achieve this outcome using different, safer approaches. I think the case offers encouragement to researchers already pursuing these goals, but I'm not sure it will help achieve them any faster."

Awakening an Exhausted Immune System

It seems as if a day doesn't go by without an interesting report from laboratory scientists claiming to cast additional light on HIV's wily ways in the human body and potential methods to stop it in its tracks. One of the most notable of 2008 involved a protein called programmed death-1 (PD-1)—and the fact that blocking it had some miraculous effects in monkeys infected with SIV, a simian version of HIV.

Two years ago, researchers reported an overabundance of PD-1 proteins on CD8 cells in people with HIV that causes essential virus-fighting components of the immune system to become fatigued and listless. The latest research, testing an anti-PD-1 antibody in nine monkeys, found both significant reductions in viral loads and an apparent survival advantage.

"The results of the SIV experiment were not as straightforward as some of the stories made it sound, but it was still an important study," says TAG's Jefferys. "Reviving exhausted virus-specific T-cell responses has always sounded like a nice idea in theory, but this experiment is the first hint that it may actually be possible."

Fat Buster to the Fore

When it became clear in 2007 that EMD Serono's Serostim (recombinant human growth hormone) was unlikely to be approved for the treatment of HIV-related body fat accumulation, all eyes focused on the development of tesamorelin. Theratechnologies' injectable compound jump-starts the natural production of fat-busting growth hormone, but without the side effects seen in studies of Serono's agent.

This year saw the successful completion of not one, but two, Phase III tesamorelin studies. And in a

deal to put the Montreal-made product into the hands of U.S. residents, Theratechnologies struck a deal with EMD Serono to market and sell the drug.

When asked where things stand regarding the pending availability of tesamorelin, Nelson Vergel, director of Program for Wellness Restoration, expressed frustration. “It is not yet approved by the FDA pending additional data,” he says, although it is expected to get the thumbs up from the FDA sometime in 2009. “Theratechnologies has not committed to providing the drug through a pre-approval expanded access program, despite frequent demands by activists.

“Visceral fat accumulation can not only affect self image in people with HIV, but also increase cardiovascular risks and belly discomfort,” Nelson adds. “I really hope that Theratechnologies and EMD Serono work together to provide this drug to people who need it before and after FDA approval.”

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