Studies Disagree on Abacavir for Patients With High Viral Loads

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HIV-positive patients with high viral loads who start their first antiretroviral (ARV) treatment regimen with Epzicom (abacavir plus lamivudine) experience virologic failure and moderate-to-severe side effects faster than those who start with a regimen containing Truvada (tenofovir plus emtricitabine), according to early results from a federally funded AIDS Clinical Trials Group (ACTG) study reported at the XVII International AIDS Conference (IAC) in Mexico City. However, an analysis of six clinical trials reported at the conference by GlaxoSmithKline, Epzicom's manufacturer, indicates similar safety and efficacy among patients with viral loads both above and below 100,000 copies.

Background

ACTG study 5202 is a 96-week study that, since its 2005 start date, has enrolled more than 1,600 people living with HIV who had never before taken antiretroviral (ARV) drugs. The study participants have been split into four groups comparing the safety and efficacy of four popular ARV options among those starting therapy for the first time. One group started a regimen containing Epzicom and Sustiva (efavirenz), another started a regimen containing Epzicom and Norvir (ritonavir)-boosted Reyataz (atazanavir), a third started a regimen containing Truvada and Sustiva, and the last started a regimen containing Truvada and Norvir-boosted Reyataz. Each of the four groups was further split into two groups depending on whether participants had viral loads under or over 100,000 copies.

The participants, as well as the study investigators, knew whether they were taking Sustiva or Reyataz/Norvir. The rest of their treatment regimen, however, was "blinded," meaning that neither the investigators nor the participants knew whether Epzicom or TruvadaFebruary, a data and safety monitoring board (DSMB) overseeing ACTG study 5202 recommended participants who began treatment with viral loads in excess of 100,000 copies be told which NRTI combination they were allotted to and provided with the option of switching to Truvada or an alternative NRTI regimen. In other words, the study was partially unblinded.

In a letter to study investigators and participants, the DSMB explained that the rates of virologic success and side effects differed among those who entered the study with viral loads over 100,000 copies, depending on whether they were receiving Epzicom or Truvada. The actual results, however, were not made available to the public until last week's conference.

The study remains blinded for patients who began with viral loads below 100,000 copies. The

DSMB has not reported any significant differences in this group of patients, and final results will be reported and published at a later date.

ACTG 5202: The Early Results

Taking the podium at IAC, ACTG 5202 study investigator Paul Sax, MD, of Harvard Medical School in Boston explained that 797 patientswas 1.89 times faster in the Epzicom group compared with the Truvada group. There were 130 moderate-to-severe side effects among Epzicom takers starting treatment with high viral loads, compared with 78 moderate-to-severe side effects in the Truvada group.

Lipid abnormalities, such as high total cholesterol, “bad” LDL cholesterol and triglycerides, were documented in 41 of the Epzicom-treated patients compared with 11 of the Truvada-treated patients. Moderate-to-severe pains or aches, liver enzyme increases and skin irritation also appeared more likely to occur in the Epzicom group versus the Truvada group.

The GSK Analysis

To either confirm or refute the findings of ACTG 5202, Keith Pappa, PharmD, of GlaxoSmithKline, and his colleagues reanalyzed data from six randomized studies in which abacavir and lamivudine were used as the “backbone” NRTI component, including one ongoing trialeither above or below 100,000 copies. Similarly, the researchers defined virologic failure as a confirmed viral load at or above 1,000 copies between weeks 16 and 24 of treatment, or a viral load at or above 200 from week 24 onward.

At 48 weeks in all six studies, 87 to 95 percent of all patients in the analysis did not meet the definition for virologic failure, with no major differences between those with viral loads above 100,000 copies compared with those starting treatment with viral loads below 100,000 copies.

While one of the conference delegates suggested during the question-and-answer period that there was a “trend toward” less virologic success among patients with higher viral loads in the studies, Dr. Pappa reiterated that there were no statistically significant differences between the low- and high-viral load groups, meaning that the observed differences were all small enough to have occurred by chance.

The HEAT study enrolled 688 patients, 393 of whom had viral loads of at least 100,000 upon entering the trial. Data from that study show that 87 percent of those with high viral loads starting treatment with Epzicom had undetectable viral loads after 48 weeks, compared with 90 percent of those in the Truvada group. This difference, however, was not statistically significant5 percent of patients with high pre-treatment viral loads who received Epzicom, compared with 8 percent of those who received Truvada.

It is not yet clear how to reconcile the differences between ACTG 5202 and the other clinical trials involving abacavir and lamivudine.

One important difference, Sax noted, was that the total number of patients in HEAT

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