Truvada vs. Epzicom: The Debate Goes On

November 3, 2008 By Tim Horn

A handful of presentations at the 2008 joint meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) and the Infectious Disease Society of America (IDSA) did little to settle the debate regarding the effectiveness of Epzicom (abacavir/lamivudine) compared with Truvada (tenofovir/emtricitabine). One presentation indicated that Epzicom may be the better bet for patients starting treatment with viral loads below 100,000 copies, and another indicated that Truvada is more likely to keep viral loads undetectable for 48 weeks when used with Norvir (ritonavir)-boosted protease inhibitors.

Until very recently, Truvada and Epzicom were both listed as "preferred" nucleoside reverse transcriptase inhibitors (NRTIs) for first-time treatment takers—usually combined with a Norvir-boosted PI or a non-nucleoside reverse transcriptase inhibitor (NNRTI)—in HIV treatment guidelines maintained by the U.S. Department of Health and Human Services (DHHS). On November 3, new DHHS guidelines downgraded Epzicom to "alternative" standing, leaving Truvada as the only preferred option, due in part to recent data from AIDS Clinical Trials Group (ACTG) study 5202 concluding that HIV-positive patients starting treatment for the first time with viral loads above 100,000 were more likely to experience virologic failure when using Epzicom compared with Truvada. However, a GlaxoSmithKline (GSK) analysis of six clinical trials reported at this summer's International AIDS Conference in Mexico City indicated similar efficacy among patients with high pre-treatment viral loads.

Additional research reported at ICAAC/IDSA yielded similarly confusing results.

The HEAT Study

Ninety-six week data from the HEAT study, a head-to-head comparison of Epzicom and Truvada, each with Kaletra (lopinavir/norvir), continues to show that treatment failure rates are similar in both groups of patients being studied. And while the latest analysis adds further credence to the results of ACTG 5202, indicating a Truvada advantage for those beginning treatment with high viral loads, HEAT also concluded that patients with viral loads below 100,000 copies were more likely to benefit virologically from Epzicom for 96 weeks.

The study randomized 343 treatment-naïve patients to receive Kaletra/Epzicom and 343 to receive Kaletra/Truvada. By 96 weeks, 14 percent of patients in both groups experienced virologic

failure—defined as a viral load that failed to fall below 200 copies by 24 weeks or a viral load that became detectable again after going undetectable by week 24—while receiving their assigned treatment regimen.

To make sense of the failures seen in the study, the researchers analyzed data involving the 49 patients who experienced virologic failure in the Epzicom group and the 49 patients who experienced virologic failure in the Truvada group.

Interestingly, while black patients accounted for 36 percent of the full study, they accounted for 56 percent of those with virologic failure. Forty-five percent of those who stopped responding effective to Epzicom were black, compared with 63 percent of those who stopped responding effective to Truvada.

Among those who entered HEAT with viral loads below 100,000 and stopped responding to treatment, virologic failure was documented in 63 percent of those in the Truvada group, compared with 41 percent of those in the Epzicom group. Among those with pre-treatment viral loads between 100,000 and 250,000 copies, failure rates were similar: 19 percent versus 18 percent, respectively. Truvada was more likely to push and keep viral loads undetectable in those with viral loads between 250,000 and 500,000 copies and above 500,000 copies, with 18 percent and 22 percent of those failing Epzicom in these pre-treatment categories, compared with 4 percent and 15 percent of those treated with Truvada and very high pre-treatment viral loads.

The HEAT researchers also reported that the M184V mutation in HIV's reverse transcriptase, which confers high-level resistance to the lamivudine in Epzicom and the emtricitabine in Truvada, was more likely to occur in patients who failed Truvada compared with Epzicom.

Twelve-Study Review

A review of 12 clinical trials comparing the active ingredients in Epzicom with Truvada, reported at ICAAC/IDSA by a team of independent researchers, indicates that Truvada is more likely to keep viral load below 50 copies after 48 weeks of treatment than Epzicom, at least when both regimens are combined with a Norvir-boosted PI for first-line therapy. However, the fact that many of these studies were conducted before the discovery of the HLA-B*5701 assay—a genetic test to prevent abacavir treatment in patients with a high risk of an allergic reaction to the drug and thus more likely to "fail" treatment in the clinical trials—may have contributed to this difference.

The studies reviewed in the ICAAC/IDSA presentation involved 4,895 patients allotted to 21 different treatment groups involving either tenofovir plus emtricitabine or abacavir plus lamivudine—some studies predated the two-in-one Truvada and Epzicom formulations—in combination with either Norvir-boosted Reyataz (atazanavir), Lexiva (fosamprenavir), Invirase (saquinavir) or Kaletra. The results from these studies were reported between January 2000 and March 2008.

In studies involving Norvir-boosted Reyataz, 79 percent of those taking tenofovir/emtricitabine,

compared with 77 percent of those taking abacavir/lamivudine, had viral loads below 50 copies after 48 weeks. In studies of Norvir-boosted Lexiva, rates were 75 percent and 67 percent, respectively. And in studies of Kaletra, rates were 74 percent and 66 percent respectively. No differences with Norvir-boosted Invirase were reported.

The researchers found higher rates of undetectable viral loads after 48 weeks with tenofovir/emtricitabine compared with abacavir/lamivudine in patients with viral loads both above and below 100,000 copies with Kaletra or Norvir-boosted Reyataz or Lexiva. Among those with pre-treatment viral loads below 100,000 copies, 79.1 percent receiving tenofovir/emtricitabine, versus 69.5 percent of those receiving abacavir/lamivudine, had viral loads below 50 copies after 48 weeks. As for those with pre-treatment viral loads above 100,000 copies, rates of viral load suppression were lower in both groups, but still better in the tenofovir/emtricitabine group: 70.6 percent versus 65.9 percent, respectively. These differences were statistically significant, meaning that they were too great to have occurred by chance.

It is important to note that a number of patients randomized to abacavir/lamivudine in these studies experienced a suspected allergic reaction to abacavir and, as a result, discontinued treatment. This, the researchers point out, may have contributed to the lower response rates in the abacavir/lamivudine groups.

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