Long-Term Benefits and Risks of Kaletra Monotherapy Explored in Two Studies

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More than 10 years after combination HIV treatment was heralded as the one and only way to treat HIV, data continue to emerge suggesting that monotherapy—the use of just one HIV drug—may be a possibility. Long-term results from two Kaletra (lopinavir/ritonavir) studies, reported at the 2008 joint meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) and the Infectious Disease Society of America (IDSA), continue to show that there may be potential for two monotherapy approaches.

Switching From Triple-Drug Kaletra Therapy to Kaletra Monotherapy

The first study, known as OK04, enrolled 198 HIV-positive people who had been on a stable regimen containing Kaletra plus two NRTIs for about 18 months. Upon entering the trial, the patients were divided into two groups: One group remained on the triple combination, while the other withdrew the two NRTIs and continued Kaletra by itself.

According to 96-week OK04 data presented at the 11th European AIDS Conference in Madrid last year, people who simplified their treatment by going solo with Kaletra—with reintroduction of NRTI treatment as needed—appeared to do just as well virologically as those who remained on triple-drug treatment. The percentage of people with a viral load of less than 50 copies after 96 weeks was 77 percent in the monotherapy group and 78 percent in the triple combination group. This meant that switching to monotherapy, after virus was well controlled, was not statistically inferior to remaining on triple combination therapy.

At ICAAC/IDSA, Federico Pulido, MD, of the Hospital 12 de Octubre in Madrid and his colleagues presented data involving the 100 patients originally randomized to Kaletra monotherapy and followed for 144 weeks (nearly three years). Seventy-three of these patients completed all 144 weeks of Kaletra monotherapy; 17 experienced viral load rebounds while on monotherapy (15 of whom restarted their NRTIs), nine dropped out of the study, two died, and one changed his treatment regimen entirely.

According to the strict “intent-to-treat” analysis, in which those who dropped out or reintroduced NRTI therapy were counted as failures, 71 percent of the patients on Kaletra monotherapy had undetectable viral loads (below 50 copies) after 144 weeks. A comparison between those who switched from triple-drug treatment to Kaletra monotherapy after 96 weeks and those who

remained on Kaletra monotherapy for 144 weeks was not reported.

By way of conclusion, Dr. Pulido and his colleagues write: “This result supports the durability of [Kaletra] monotherapy and is consistent with the long-term follow-up of our pilot trial in which 66.7 percent of patients randomized to [Kaletra] monotherapy remain on monotherapy and with [viral loads] less than 50 copies.” The study they refer to was recently published in the Journal of Antimicrobial Chemotherapy.

Starting With Kaletra Monotherapy

Starting treatment with Kaletra monotherapy—without NRTIs or other antiretrovirals, as was employed in the OK04 study—has produced mixed results in clinical trials. In 2006, for example, data from the French MONARK study presented at the 15th International Drug Resistance Workshop in Sitges indicated that 20 percent of people taking Kaletra monotherapy either failed to fully suppress virus or experienced a viral load rebound, compared with only 2 percent of people taking Kaletra plus two NRTIs.

At ICAAC/IDSA, Joseph Gathe, MD, a private physician based in Houston—a Kaletra monotherapy pioneer—and his colleagues reported 96-week data from an open-label study evaluating single-agent therapy with Kaletra in 39 HIV-positive patients starting treatment for the first time. Of note, the study conducted by Dr. Gathe’s group did not contain a control group of patients taking standard triple-drug treatment.

Thirty-four of the 39 patients enrolled completed 96 weeks of treatment, 33 of whom remained on Kaletra monotherapy for the entire time.

After 96 weeks of Kaletra monotherapy, 74 percent of the patients enrolled—according to a strict intent-to-treat analysis of the study—had viral loads below 75 copies. While it is difficult to compare the results of different studies, this 96-week result is similar to those seen in clinical trials evaluating three-drug regimens containing Kaletra.

Dr. Gathe noted that viral load rebounds in the study, if the occurred, were often associated with documented or suspected poor adherence. In the first 48 weeks of the study, four of six rebounding patients were able to push their viral loads back down to undetectable levels after receiving adherence counseling or intensifying their Kaletra with NRTIs.

Only one patient who had a detectable viral load while on Kaletra monotherapy appeared to develop some degree of HIV resistance to the drug (rates of protease inhibitor resistance were higher in the MONARK study). Other cases of detectable viral load were believed to be associated with poor adherence and were remedied with adherence counseling or intensification of treatment with the addition of NRTIs.
It remains unclear if Kaletra monotherapy is likely to cause fewer side effects than what is typically seen with triple-drug treatment. Diarrhea occurred in 44 percent of patients in this Kaletra monotherapy study, and increases in total cholesterol, “bad” LDL cholesterol and triglycerides were noted as well.

Gathe concluded that additional analyses of this study are ongoing—including data involving ultra-sensitive drug-resistance testing and a review of the cost effectiveness of Kaletra monotherapy—and he suggested that a large study, comparing Kaletra monotherapy to standard

triple-drug treatment, is needed to further explore the potential value of this experimental treatment approach.

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