Abortion Pill for HIV? Questions Still Remain

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One of the most intriguing compounds to be studied as an HIV therapy is mifepristone, a controversial medication sold in the United States as Mifeprex® and used to chemically induce abortions in the early stages of pregnancy. While the scientific rationale behind using mifepristone as an anti-HIV agent has piqued the interest of researchers for several years, the results of a new clinical trial reported Wednesday at the 46th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in San Francisco indicate that its therapeutic potential for this indication remains unclear.

One of HIV's proteins, vpr, is used by the virus to incorporate its genetic material into the nucleus of certain immune system cells in the body. For this to happen, vpr must first bind with a cellular protein, called the glucocorticoid receptor II (GCRII). GCRII is normally activated by the hormone cortisol, which is produced by the adrenal glands situated immediately above the kidneys.

Mifepristone is approved by the U.S. Food and Drug Administration due to its ability to block progesterone, a hormone that is required during early pregnancy to maintain development of the fetus. If progesterone production is blocked, the fetus will cease development and be expelled from the uterus. It is therefore prescribed by healthcare providers to induce an abortion in women wishing to terminate their pregnancy, if taken within two months of conception.

While mifepristone was being developed for this purpose, researchers discovered that it also blocks GCRII. In turn, test tube and animal studies were conducted and found that mifepristone inhibited the interaction between vpr and GCRII and was associated with anti-HIV activity. A clinical trial involving HIV-positive people was then started in 2005, conducted by the federally funded AIDS Clinical Trials Group (ACTG).

The study, A5200, evaluated three different doses of mifepristone (75mg, 150mg, and 225mg daily) or placebo taken for a total of 28 days. The patients enrolled were required to have CD4 (T4 cell) counts above 350, viral loads above 2000, and no other use of HIV medications within 16 weeks before entering the trial.

Fifty-six HIV-positive people, including one female, were enrolled. A total of 45 patients were

included in the analysis.

After 28 days of treatment, cortisol levels in the bloodstream were increased in the mifepristone-treated patients. This was interpreted to mean that the drug does have biological activity against GCRII, as blockage of the receptor would be expected to cause an increase in the production of cortisol. However, mifepristone did not have an effect on the patients' viral loads or CD4 counts. After 28 days of treatment, viral load did not significantly decrease, nor did CD4 cell counts significant increase, compared to those who took placebo.

Despite the study's discouraging results, the researchers remain optimistic. Based on the encouraging results seen in animal studies, compounded by the drug's safety in the ACTG study, a study exploring higher doses of mifepristone in HIV-positive people is planned.
