New once-daily 'Quad' pill for HIV is safe, effective alternative to traditional antiretroviral regimens

June 28 2012

A new once-daily pill combining three antiretrovirals and a booster molecule is a safe and effective alternative to two widely used drug regimens for newly diagnosed HIV-positive adults who have had no previous treatment. The findings of two large international randomized trials published in this week's Lancet also indicate that the new "Quad" pill is faster acting, doesn't have the neuropsychiatric side effects associated with other combinations, and could improve compliance with treatment.

"Patient adherence to medication is vital, especially for patients with HIV, where missed doses can quickly lead to the virus becoming resistant to medication. Older HIV treatment regimens involve taking several pills multiple times a day", explains Paul Sax from Brigham and Women's Hospital, Harvard Medical School, lead author of the first study. "Our results provide an additional highly potent, well-tolerated treatment option, and highlight the simplicity of treatment resulting from combining several antiretrovirals in a single pill. Studies have shown that single pill treatments improve both adherence and patient satisfaction, and help prevent prescription errors, thereby reducing the likelihood of treatment failure and drug resistance."

Guidelines from the US Department of Health and Human Services currently recommend emtricitabine (FTC) and tenofovir disoproxil fumarate (TDF) in combination with a third agent—efavirenz (EFV),

one of the ritonavir-boosted (RTV) protease inhibitors darunavir or atazanavir (ATV), or the integrase inhibitor raltegravir—as the preferred regimen for adults beginning antiretroviral treatment.

The first trial randomly assigned 700 patients from centres across North America to start treatment with two different single tablet regimens—either Quad, combining the new integrase inhibitor elvitegravir (EVG) boosted with cobicistat (a new pharmacoenhancer; COBI) plus FTC/TDF, or a gold standard regimen approved by the FDA in 2006, combining EFV/FTC/TDF (also known as Atripla).

After 48 weeks of treatment, 88% of patients given Quad suppressed viral loads to undetectable levels (less than 50 copies per mL of blood), compared with 84% in the EFV/FTC/TDF group.

Adverse events that led to patients discontinuing treatment were infrequent and similar in both groups. Mild nausea was more common with Quad, but patients were less likely to have dizziness, abnormal dreams, insomnia, and rash compared with the EFV/FTC/TDF regimen.

The second trial included 708 treatment-naïve adults from 146 medical centres across Australia, Europe, North America, and Thailand. Patients were randomly assigned to receive once-daily Quad or a popular and recommended twice-daily combination of ritonavir-boosted atazanavir (ATV/RTV) plus FTC/TDF.

The primary endpoint, to achieve viral levels below 50 copies per mL of blood by week 48, was reached by 90% of people in the Quad group compared with 87% in the ATV/RTV/FTC/TDF group.

The safety of the two regimens was also similar with only 3.7% of patients stopping treatment in the Quad group and 5.1% of patients in the ATV/RTV/FTC/TDF group. However, a higher number of kidney

complications were reported in patients taking Quad compared with the other HIV treatments.

"If approved by regulatory agencies, the Quad would be the first once-daily single-tablet regimen containing an HIV integrase inhibitor. Based on the safety and efficacy results from the two large-scale clinical studies, Gilead believes the Quad represents a potentially important new treatment option for a wide range of HIV patients initiating therapy", concludes Brian Kearney, one of the authors from Gilead Sciences who developed the Quad pill.

In a linked Comment, Rik Schrijvers and Zeger Debyser from the Katholieke Universiteit Leuven in Belgium say: "[The studies] show that Quad has high efficacy and a good tolerability profile, with the limitations of potential drug interactions and a need to be taken with food. The underrepresentation of women in these studies, and absence of long-term safety data (especially for renal toxic effects) and resistance data, warrant further research."

More information: www.thelancet.com/journals/lan … (12)60917-9/abstract
www.thelancet.com/journals/lan … (12)60918-0/abstract

Provided by Lancet