Is pre-exposure prophylaxis an effective means of reducing the number of new HIV infections?

In my previous posting from the 2015 Conference on Retroviruses and Opportunistic Infections (CROI), I mentioned an impressive statistic: If, worldwide, we could diagnose 90% of those infected with HIV, and get 90% of them on therapy, mathematical models suggest that there would be a 70% decrease in the numbers of new infections. This is just one example of the magnitude of the effect of “treatment as prevention.” Currently, it is estimated that only 20% of those infected are receiving therapy (40% of the only 50% known to be HIV-infected).

Clearly there is much work to be done. Nevertheless, treatment as prevention, especially among discordant monogamous couples, has been shown on a large scale to be over 95% effective. The same cannot be said, at least consistently on a large scale, with PrEP (Pre-exposure prophylaxis).

PrEP, on a smaller scale, does seem to reduce the number of new infections (compared with placebo) by the same order of magnitude (70% or so) that large scale-up efforts of antiretroviral treatment of those known to be HIV-infected are attempting to achieve. Not surprisingly then, much of today’s conference was devoted to the issue of PrEP.

Here is what we learned:

1. In the Pragmatic Open-Label Randomised Trial of Preexposure Prophylaxis (PROUD) Study, 545 men who have sex with men (MSM), average age of 35, were randomized to take daily Truvada (tenofovir/emtricitabine) or nothing. In the group assigned to daily Truvada, there was an 86% reduction in cases of HIV (19 in the placebo group versus 3 in the Truvada group) over 48 weeks. The incidence of other STDs did not differ between the two groups.

2. “On demand” PrEP (Truvada 2 pills 2 – 24 hours before sex and again 24 hours and 48 hours later) was 86% effective in reducing the incidence of new HIV infections (versus placebo) in the 400 MSM participating in this 8-month randomized, double-blind study.

3. In a mathematical modeling study of all populations of at-risk persons in San Francisco (“realistic model”), the investigators concluded that the incidence (new cases of HIV) would fall by 30% if 6400 people were on PrEP. However, city-wide, getting to less than 50 new cases per year would require that diagnosis rates increase to over 99%, with 90% achieving maximal viral suppression, “at which point PrEP’s impact on HIV incidence decreases because exposure to untreated HIV infection would be rare.”

4. Pericoital prophylaxis with 1% tenofovir gel was not effective in preventing new HIV infections among the 2000 South African women randomized to receive the tenofovir gel versus placebo.

5. In the open-label extension of one of the original PrEP trials to demonstrate efficacy (iPrEx), long-term follow-up showed substantial decreases in the number of individuals using PrEP, as well as decreases in the number of individuals with effective serum levels of tenofovir to provide protection. Specifically, at 12 months, only 22% of the more than 1600 MSM offered PrEP had serum levels of tenofovir deemed to be in the “highly protective” range (approximating levels obtained with 4 or more pills per week). Similarly, in a study of awareness of, willingness to use, and barriers to the use of PrEP among white and black Atlanta-area MSMs, “theoretical protection” was predicted to occur in only 15% of the population.

Taken as a whole, these studies indicate that substantial challenges exist in the acceptability of, and adherence to, PrEP among diverse populations of individuals known to be at high risk for acquiring HIV infection. Although PrEP has the potential to substantially decrease new HIV infections, the reality is that, at least for now, other prevention efforts (eg, treatment as prevention) are more likely to have a substantial impact at the population level.
HIV assembling on the surface of an infected macrophage. Image source:...

**Disclosures:**


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