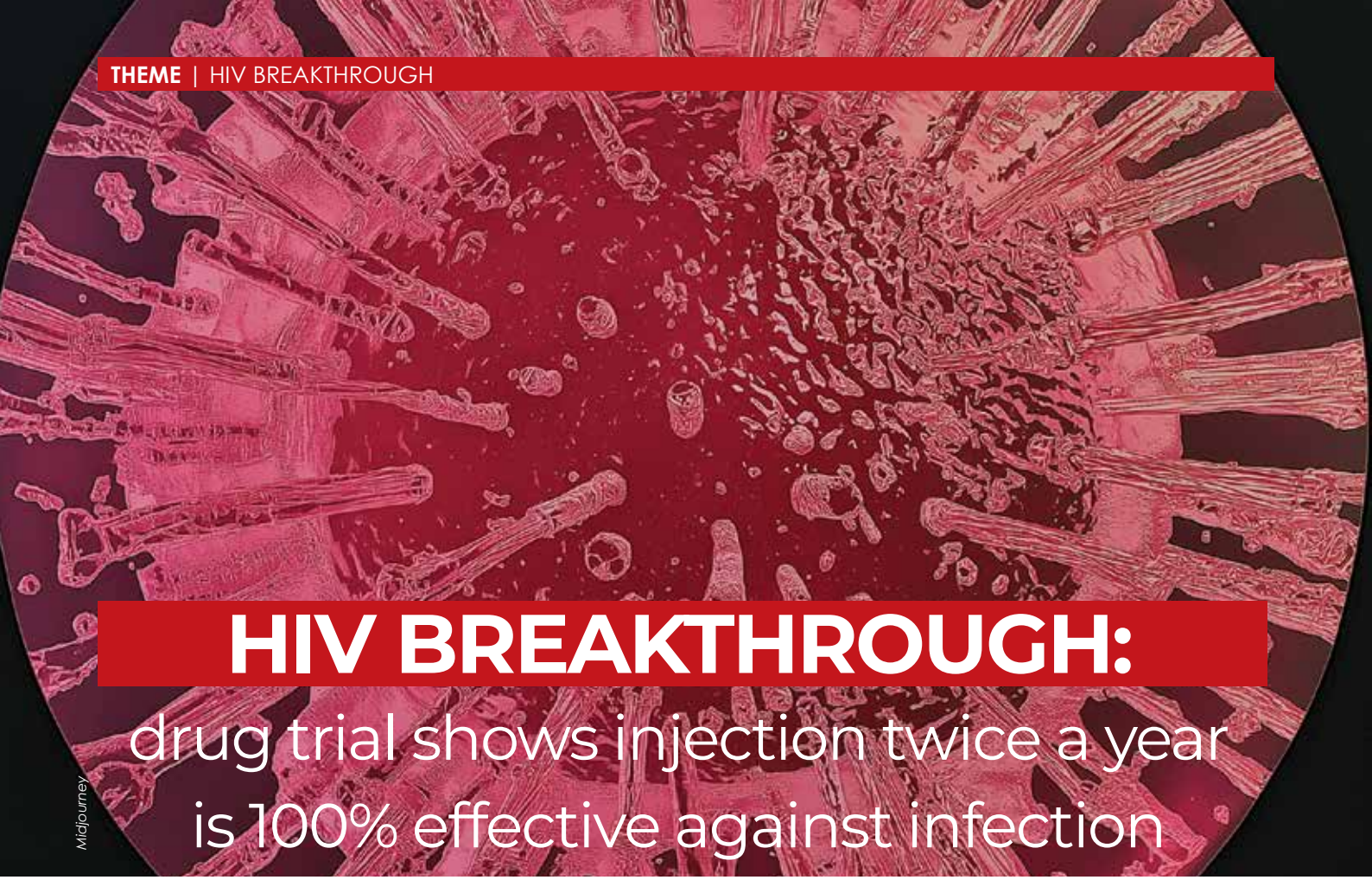

Midjourney

HIV BREAKTHROUGH:

drug trial shows injection twice a year is 100% effective against infection

A large clinical trial in South Africa and Uganda has shown that a twice-yearly injection of a new pre-exposure prophylaxis drug gives young women total protection against HIV infection. The trial tested whether the six-monthly injection of lenacapavir would provide better protection against HIV infection than two other drugs, both daily pills. All three medications are pre-exposure prophylaxis (or PrEP) drugs. Physician-scientist Linda-Gail Bekker, principal investigator for the South African part of the study, tells Nadine Dreyer what makes this breakthrough so significant and what to expect next.

Tell us about the trial and what it set out to achieve

The Purpose 1 trial with 5,000 participants took place at three sites in Uganda and 25 sites in South Africa to test the efficacy of lenacapavir and two other drugs. Lenacapavir (Len LA) is a fusion capside inhibitor. It interferes with the HIV capsid, a protein shell that protects HIV's genetic material and enzymes needed for replication. It is administered just under the skin, once every six months.

The randomised controlled trial, sponsored by the drug developers Gilead Sciences, tested several things. The first was whether a six-monthly injection of lenacapavir was safe and would provide better protection against HIV infection as PrEP for women between the ages of 16 and 25 years than Truvada F/TDF, a daily PrEP pill in wide use that has been available for more than a decade.

Secondly, the trial also tested whether Descovy F/TAF, a newer daily pill, was as effective as F/TDF. The newer F/TAF has superior pharmacokinetic properties to F/TDF. Pharmacokinetic refers to the movement of a drug into, through and out of the body. F/TAF is a smaller pill and is in use among men and transgender women in high-income countries.

The trial had three arms. Young women were randomly assigned to one of the arms in a 2:2:1 ratio (Len LA: F/TAF oral: F/TDF oral) in a double-blinded fashion. This means neither the participants nor the researchers knew which treatment participants were receiving until the clinical trial was over.

In eastern and southern Africa, young women are the population who bear the brunt of new HIV infections. They also find a daily PrEP regimen challenging to maintain, for a number of social and structural reasons. During the randomised phase of the trial, none of the 2,134 women who received lenacapavir contracted HIV. There was 100% efficiency.

By comparison, 16 of the 1,068 women (or 1.5%) who took Truvada (F/TDF) and 39 of the 2,136 (1.8%) who received Descovy (F/TAF) contracted the HIV virus.

The results at a recent independent data safety monitoring board review led to the recommendation that the trial's "blinded" phase should be stopped and all participants should be offered a choice of PrEP.

This board is an independent committee of experts who are put in place at the start of a clinical trial. They see the unblinded data at stipulated times during the trial to monitor progress and safety. They ensure that a trial does not continue if there is harm or a clear benefit in one arm over others.

What is the significance of these trials?

This breakthrough gives great hope that we have a proven, highly effective prevention tool to protect people against HIV.

There were 1.3 million new HIV infections globally in the past year. Although that is fewer than the 2 million infections seen in 2010, it is clear that at this rate we are not going to meet the HIV new infection target that UNAIDS set for 2025 (fewer than 500,000 globally) or potentially even the goal to end AIDS by 2030.

PrEP is not the only prevention tool. PrEP should be provided alongside HIV self-testing, access to condoms, screening and treatment for sexually transmitted infections and access to contraception for women of childbearing potential. In addition, young men should be offered medical male circumcision for health reasons.

But despite these options, we have not quite reached the point where we have been able to stop new infections, particularly among young people. For young people, the daily decision to take a pill, or use a condom, or take a pill at the time of sexual intercourse can be very challenging. HIV scientists and activists hope that young people may find that having to make this "prevention decision" only twice a year may reduce unpredictability and barriers.

For a young woman who struggles to get to an appointment at a clinic in a town, or who cannot keep pills without facing stigma or violence, an injection just twice a year is the option that could keep her free of HIV.

What happens now?

The plan is that the Purpose 1 trial will continue but now in an "open label" phase. This means that study participants will be "unblinded": they will be told whether they have been in the "injectable", or oral TDF, or oral TAF groups. They will be offered the choice of PrEP they would prefer as the trial continues.

A sister trial is also under way: Purpose 2 is being conducted in a number of regions including some sites in Africa among cisgender men, and transgender and nonbinary people who have sex with men. It is important to conduct trials among different groups because we have seen differences in effectiveness. Whether the sex is anal or vaginal is important and may have an impact on effectiveness.

How long until the drug is rolled out?

We have read in a Gilead Sciences press statement that within the next couple of months the company will submit the dossier with all the results to a number of country regulators, particularly the Ugandan and South African regulators. The World Health Organization (WHO) will also review the data and may issue recommendations. We hope then that this new drug will be adopted into WHO and country guidelines. We also hope we may begin to see the drug being tested in more studies to understand better how to incorporate it into real-world settings.

Price is a critical factor to ensure access and distribution in the public sector where it is badly needed. Gilead Sciences has said it will offer licences to companies that make generic drugs, which is another critical way to reduce prices. In an ideal world, governments will be able to purchase this affordably and it will be offered to all who want it and need protection against HIV.

Article written by Nadine Dreyer for TheConversation.com and first published here.

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