



Prevention: Longer-Acting PrEP

A once-yearly injectable and a once-monthly pill could be game changers for HIV prevention.

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A once-yearly injectable and a once-monthly pill—both now in late-stage trials—could be game changers for HIV prevention. Twice-yearly lenacapavir (Yeztugo) PrEP administered every six months was highly effective in two large trials, but longer-lasting versions might offer protection for a full year. Using a population pharmacokinetic model to guide dose selection, researchers at Gilead Sciences projected that a 3,000 mg dose of an intramuscular formulation would yield a 52-week trough concentration exceeding the 26-week trough level of the approved twice-yearly subcutaneous formulation. Once-yearly lenacapavir PrEP is now being tested in the Phase III PURPOSE 365 trial. Similarly, Merck researchers used pharmacokinetic modeling to select a dose for MK-8527, its nucleoside reverse transcriptase translocation inhibitor PrEP candidate. An 11 mg oral dose reached a protective concentration within one hour, provided coverage for a month and had a seven-day dosing window. The Phase III EXPrESSIVE-10 and EXPrESSIVE-11 trials are now recruiting participants.

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