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Research Article

Cabotegravir: A Novel Drug For Prophylaxis Of HIV/AIDS As Pre-Exposure Prophylaxis (PREP)

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Abstract

Background: Cabotegravir is a novel integrase strand transfer inhibitor (INSTI) developed for HIV-1 prophylaxis as pre-exposure prophylaxis (PrEP). Given the global burden of HIV/AIDS, there is a critical need for effective, long-acting PrEP options. Cabotegravir's long-acting injectable formulation offers potential advantages over daily oral PrEP regimens, addressing issues related to adherence and resistance.

Method: This review synthesizes the results of key clinical trials, including HPTN 083 and HPTN 084, which evaluated the efficacy, safety, and acceptability of long-acting cabotegravir in diverse populations at risk of HIV infection. The pharmacokinetic properties, mechanism of action, and comparative effectiveness to existing PrEP options are discussed.

Results: Clinical trial data demonstrate that long-acting cabotegravir significantly reduces the risk of HIV acquisition compared to oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC). In HPTN 083, among men who have sex with men and transgender women, cabotegravir showed a 66% reduction in HIV incidence compared to TDF/FTC. HPTN 084 reported an 89% reduction in HIV risk among cisgender women. Cabotegravir was generally well-tolerated, with injection site reactions being the most common adverse event. Its long half-life supports dosing every eight weeks, which enhances adherence compared to daily oral PrEP.

Conclusions: Cabotegravir represents a significant advancement in HIV prevention, offering an effective, long-acting alternative to daily oral PrEP. Its high efficacy, favorable safety profile, and less frequent dosing schedule address major barriers to PrEP adherence. Future research should focus on implementation strategies, long-term safety, and cost-effectiveness to optimize its use in diverse populations at risk of HIV infection.

Keywords: Cabotegravir, HIV prevention, pre-exposure prophylaxis (PrEP), long-acting injectable, HPTN 083, HPTN 084, adherence, HIV/AIDS.

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Introduction

Human Immunodeficiency Virus (HIV) remains a significant global health challenge, with millions of new infections occurring annually. Pre-exposure prophylaxis (PrEP) has emerged as a pivotal strategy in reducing HIV transmission among high-risk populations. Traditional PrEP regimens involve daily oral administration of antiretroviral drugs, such as tenofovir disoproxil fumarate/emtricitabine (TDF/FTC). While effective, daily oral PrEP faces challenges related to adherence, stigma, and potential drug resistance. To address these issues, cabotegravir, a long-acting injectable integrase strand transfer inhibitor (INSTI), has been developed. This article reviews the clinical efficacy, safety, and potential impact of cabotegravir as a novel PrEP option (1-3).

Methods

A comprehensive review of the literature was conducted, focusing on pivotal clinical trials such as HPTN 083 and HPTN 084. These trials investigated the efficacy, safety, and acceptability of long-acting cabotegravir in preventing HIV infection. Data from these trials were analyzed to compare cabotegravir's performance against standard oral PrEP regimens (4-5).

Pharmacokinetics and Mechanism of Action

Cabotegravir is an INSTI that inhibits HIV integrase, an enzyme crucial for viral replication. Its long half-life allows for extended dosing intervals, making it suitable for long-acting injectable formulations (6). Pharmacokinetic studies indicate that cabotegravir maintains therapeutic drug levels for up to eight weeks following an injection, supporting its use as a bi-monthly PrEP option (8,10).

Results

HPTN 083 Trial: This trial included men who have sex with men (MSM) and transgender women. Participants were randomized to receive either long-acting cabotegravir injections every eight weeks or daily oral TDF/FTC. The results showed that cabotegravir was significantly more effective, reducing HIV incidence by 66% compared to TDF/FTC. The trial highlighted cabotegravir's superior efficacy in maintaining consistent drug levels and overcoming adherence challenges associated with daily oral PrEP (11,12).

HPTN 084 Trial: Focused on cisgender women, this trial similarly compared long-acting cabotegravir to daily oral TDF/FTC. The findings were striking, with cabotegravir reducing HIV risk by 89%. This high efficacy is particularly important for populations where adherence to daily medication can be more challenging due to social and economic factors (1,5-7).

Safety and Tolerability

Cabotegravir was generally well-tolerated across both trials. The most common adverse events were injection site reactions, which were typically mild to moderate and decreased in frequency over time. No significant differences in severe adverse events were noted between the cabotegravir and TDF/FTC groups, indicating a favorable safety profile for long-acting cabotegravir (10-12).

Discussion

The introduction of long-acting cabotegravir marks a significant advancement in HIV prevention strategies. Its efficacy in diverse populations, coupled with a less frequent dosing schedule, addresses key barriers to PrEP adherence. The injectable formulation also reduces the risk of drug resistance, as consistent drug levels are maintained without reliance on daily pill-taking.

Implementation and Future Research

While the clinical benefits of cabotegravir are clear, several implementation challenges remain. Ensuring access, particularly in low-resource settings, requires attention to cost, healthcare infrastructure, and education. Additionally, long-term safety data and studies on potential drug interactions are needed to fully understand the implications of widespread cabotegravir use.

Conclusions

Cabotegravir represents a promising alternative to daily oral PrEP, offering high efficacy, a favorable safety profile, and improved adherence potential. Its role in reducing the global burden of HIV/AIDS could be transformative, particularly for populations facing significant barriers to daily medication adherence. Future research should focus on optimizing delivery strategies, monitoring long-term outcomes, and ensuring equitable access to this novel HIV prevention tool.

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