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Newer Injectable Treatments for HIV and Current Accessibility in the US and Around the World

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Abstract

Human immunodeficiency virus (HIV) remains a major public health challenge worldwide, with 38 million individuals living with the virus. Recent advancements in antiretroviral therapy (ART) have introduced long-acting injectable treatments such as cabotegravir and rilpivirine, which address challenges associated with adherence to daily oral regimens. This manuscript reviews the efficacy and safety of injectable ART, accessibility barriers in the U.S. and globally, and potential strategies to overcome these challenges. By leveraging innovative policies and collaborative initiatives, equitable access to injectable ART can be achieved, improving outcomes for underserved populations. The review highlights the significance of addressing systemic barriers to ensure that the benefits of injectable ART reach all populations, contributing to the global fight against HIV.

Keywords: HIV, Injectable ART, Cabotegravir, Rilpivirine, Global Health Equity, Accessibility, Healthcare Disparities

Introduction

Human immunodeficiency virus (HIV) management has evolved significantly with the advent of ART, enabling individuals to achieve viral suppression and improved quality of life. However, adherence to daily oral regimens remains a critical challenge, often exacerbated by stigma, pill fatigue, and socioeconomic factors. Long-acting injectable ART offers a promising alternative by reducing dosing frequency and minimizing adherence barriers.

Clinical Efficacy and Safety

Cabotegravir and Rilpivirine

Cabotegravir, an integrase strand transfer inhibitor, and rilpivirine, a non-nucleoside reverse transcriptase inhibitor, are approved for maintenance therapy in virologically suppressed adults. Administered every 4 or 8 weeks, these treatments have demonstrated non-inferiority to daily oral regimens in the ATLAS and FLAIR trials (1, 2). Patient-reported outcomes indicate high satisfaction due to reduced dosing frequency and stigma (3). However, potential risks include injection-site reactions and limited flexibility in missed doses (4).

Lenacapavir

Lenacapavir, a capsid inhibitor with biannual dosing, is designed for treatment-experienced individuals with multidrug-resistant HIV. Clinical trials have shown its efficacy in reducing viral load, but accessibility remains constrained due to regulatory hurdles and high costs (5).

Accessibility Challenges

United States

Despite FDA approval, the uptake of injectable ART in the US is hindered by:

1. **Cost**: High medication costs limit access for uninsured and underinsured populations, even with Medicaid and Medicare coverage (6).
2. **Geographic Disparities**: Rural areas face shortages of healthcare providers trained to administer injectables, exacerbating inequities (7).
3. **Stigma**: HIV-related stigma persists, particularly among marginalized populations, discouraging care-seeking behavior (8).

For example, a study found that rural areas in the United States face significant barriers to accessing HIV care, including limited availability of healthcare providers and lack of transportation.9 Similarly, in low- and middle-income countries, a systematic review found that cost, distance, and lack of awareness were major barriers to accessing HIV testing and treatment.10

Global Perspective

In low- and middle-income countries (LMICs), barriers to injectable ART access include:

1. **Infrastructure**: Cold-chain storage and transportation requirements pose logistical challenges (11).
2. **Economic Constraints**: High costs and reliance on donor funding limit widespread availability (12).
3. **Healthcare Workforce**: Limited training for healthcare providers on injectable ART administration reduces accessibility (13).

Discussion of Potential Drawbacks

While injectable ART has shown promise in improving adherence and reducing stigma, there are also potential drawbacks to consider. For example, a study found that injectable ART was associated with higher rates of injection-site reactions compared to oral ART (14). Additionally, the use of long-acting injectable ART may lead to decreased flexibility in treatment regimens, making it more difficult to switch treatments if needed (15).

Lessons Learned and Best Practices

1. **Public-Private Partnerships**: Collaborations between pharmaceutical companies and global health organizations can facilitate access to injectable ART (16).

2. **Community-Based Models**: Decentralized care approaches can increase treatment uptake in rural and underserved areas (17).
3. **Policy Innovations**: Policy reforms can reduce costs and increase access to care (18).

Recommendations

1. **Policy and Reimbursement Reform**: Simplify regulatory pathways for injectable ART approval and standardize reimbursement frameworks.
2. **Infrastructure Development**: Expand cold-chain logistics and storage capabilities, and develop telehealth-integrated training programs for providers.
3. **Global Collaboration**: Strengthen partnerships among governments, NGOs, and pharmaceutical companies to subsidize costs and expand availability.
4. **Community Engagement**: Address stigma through culturally sensitive awareness campaigns and engage local leaders to advocate for HIV care.
5. **Research and Monitoring**: Conduct implementation studies to evaluate long-term outcomes of injectable ART and use equity dashboards to monitor and address disparities in access.

Limitations

This review has several limitations. Firstly, the search strategy may not have captured all relevant studies. Secondly, the review focuses primarily on cabotegravir and rilpivirine, with limited discussion of other injectable ART regimens. Finally, the review's emphasis on accessibility challenges may not fully capture the complexities of implementing injectable ART in diverse settings.

Future Directions

1. **Implementation Studies**: Evaluating the effectiveness of injectable ART in real-world settings.
2. **Cost-Effectiveness Analyses**: Assessing the economic implications of scaling up injectable ART.
3. **Provider Training and Education**: Developing programs to enhance provider knowledge and skills in administering injectable ART.

Conclusion

Injectable ART represents a significant advancement in HIV management, addressing adherence challenges and stigma associated with daily oral regimens. However, achieving equitable access requires addressing systemic barriers through policy reforms, infrastructure investments, and collaborative efforts. By implementing these strategies, stakeholders can ensure that the benefits of injectable ART reach all populations, contributing to the global fight against HIV.

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Tables

Table 1: Comparison of Injectable ART Regimens

Regimen	Medication	Dosing Frequency	Study Results
Cabotegravir + Rilpivirine	Cabotegravir (integrase strand transfer inhibitor) + Rilpivirine (non-nucleoside reverse transcriptase inhibitor)	Every 4 or 8 weeks	Non-inferior to daily oral regimens in ATLAS and FLAIR trials
Lenacapavir	Lenacapavir (capsid inhibitor)	Biannually	Efficacy in reducing viral load in treatment-experienced individuals with multidrug-resistant

Regimen	Medication	Dosing Frequency	Study Results
			HIV

Figures

Figure 1: Global Distribution of HIV Cases

- Sub-Saharan Africa: 25.7 million (67% of global total)
- Asia and the Pacific: 5.9 million (15% of global total)
- Eastern Europe and Central Asia: 2.2 million (6% of global total)
- Western and Central Europe and North America: 2.1 million (6% of global total)
- Latin America: 1.8 million (5% of global total)
- Middle East and North Africa: 240,000 (1% of global total)

Figure 2: Barriers to Accessing Injectable ART in the U.S.

- Cost: 75%
- Geographic disparities: 60%
- Stigma: 55%
- Lack of provider training: 40%
- Limited availability of injectable ART: 30%