Long Acting Injectable ART to Improve Adherence: Aspirations and Perils

Aadia Rana, MD
Associate Professor of Medicine
University of Alabama-Birmingham School of Medicine
13th International Conference on HIV Treatment and Prevention Adherence
June 8, 2018
Disclosures

• K23 Career Developmental Grant from National Institute of Mental Health

• Discussing the use of the following drugs that are not FDA approved:
  • Oral cabotegravir
  • Long-acting cabotegravir injectable
  • Long-acting rilpivirine injectable
HIV Care Continuum, United States, 2014

An estimated 1.1 million people are living with HIV in the United States.

<table>
<thead>
<tr>
<th>% of all people living with HIV</th>
<th>Diagnosed</th>
<th>Receiving Care</th>
<th>Retained in Care</th>
<th>Virally Suppressed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>85%</td>
<td>62%</td>
<td>48%</td>
<td>49%</td>
</tr>
</tbody>
</table>

Using HIV Surveillance Data to Support the HIV Care Continuum

Skarbinski et al. JAMA Intern Med 2015;175
Assessing Barriers to Care and Treatment

- Demographics
- Substance Use
- Mental Health
- Poverty
- Stigma
- Forgetting!
- Medication Side Effects

Adherence
Interventions

• ARTAS-Strengths based/Intensive Case Management
• Patient Navigation
• Enhanced Personal Contact
• Conditional Economic Incentives

Outcomes at 6 months

- Viral Suppression: Usual Treatment (p=0.03), Navigation (p=0.003), Navigation + Incentives
- Medical Visits: Usual Treatment, Navigation, Navigation + Incentives

Metsch LR et al. Effect of Patient Navigation With or Without Financial Incentives on Viral Suppression Among Hospitalized Patients With HIV Infection and Substance Use A Randomized Clinical Trial. JAMA 2016
Could LA ART have a role in addressing some of these barriers?

• Directly-Observed Therapy

• Intolerant of oral medications

• Competing Responsibilities

• Stigma
  
  • At the beginning I thought...Oh my God...I hope I get over this depression. But, my God...I hope I won’t be taking these pills all my life. Then I went on to the injectable phase...and it was like I saw the light. And I said, God...how easy and convenient this is. It was like seeing the light. –Spain, Male trial participant

  • I love it because I don't have to take a daily medication, so that's just one less thing on my plate that I have to worry about... I definitely feel there's less pressure. I like the injection because it's not a daily, in my face, I have to do this. –U.S., Female trial participant

  • In reality, taking the pill everyday keeps it [HIV] present ...and the shot is just once a month...you remember it when you come in and the rest of the time you can basically forget it. –Spain, Male trial participant

Challenges with the use of LA ART

• Induction period on oral ART

• 2 drug ART regimen with rilpivirine and cabotegravir: limited to those WITHOUT an extensive history of resistance

• Long half-life of injectables: Risk of development of resistance

• Side-effects to Injections

• Cost

• Unstudied populations, Women of Child Bearing Potential
ACTG 5359
A Phase III Randomized-Control Trial to Evaluate Long-Acting Antiretroviral Therapy in Non-adherent HIV-Infected Individuals

Co-Chairs: Aadia Rana, Jose Castillo-Mancilla
Co-Vice Chairs: Raphael J. Landovitz, Karen Tashima
Investigators: Omar Galárraga (Behavioral Economist), Michael Stirratt (NIMH), Steve Shoptaw (NIDA), David Wohl
Pharmacologists: Adriana Andrade, Ed Acosta, Gene Morse
SDAC: Summer Zheng, Jeremiah Perez
DAIDS: Karin Klingman, Tia Morton
CTS: Mwenda Kudumu
CSS: Laurency Gaston
Industry Reps: Kim Smith (Viiv), Paul Wannamaker (Viiv), Viviam Cannon (Janssen)
Field Rep: Becky Straub (UNC)
A5359 Eligibility

• ART-experienced, HIV-infected males and non-pregnant females ≥18 years of age with:
  • HIV-1 RNA >200 copies/mL
  • Evidence of non-adherence according to at least one of the following criteria:
    • Poor virologic response within 18 months prior to study entry (defined as $< 1 \log_{10}$ decrease in HIV-1 RNA or HIV-1 RNA >200 copies/mL at two time points at least 4 weeks apart) in individuals who have been prescribed ART for at least 6 consecutive months.
    • Loss to clinical follow-up within 18 months prior to study entry with ART non-adherence for ≥6 consecutive months. Lost to clinical follow-up is defined as either no contact with provider or missed 2 or more appointments in a 6-month period. ART non-adherence is defined as a lapse in ART ≥7 days (consecutive or non-consecutive), in the 6-month period where they were lost to clinical follow-up per participant report.
  • No evidence of any clinically relevant RPV or INSTI resistance-associated mutations (historically or upon screening).
  • Ability of site clinician, in conjunction with participant, to construct a ≥3-drug ART regimen with ≥2 drugs predicted to be fully active, including a boosted PI/cobi and/or an INSTI.
A 5359 Study Design

**Study entry week**

**Conditional Economic Incentives**

<table>
<thead>
<tr>
<th>Step 1, Week</th>
<th>Milestone</th>
<th>Incentive</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Completed visit</td>
<td>$75.00</td>
</tr>
<tr>
<td>4</td>
<td>HIV-1 RNA &gt;1 log₁₀ drop</td>
<td>$75.00</td>
</tr>
<tr>
<td>8</td>
<td>HIV-1 RNA &gt;2 log₁₀ drop</td>
<td>$75.00</td>
</tr>
<tr>
<td>12</td>
<td>HIV-1 RNA &lt;200 copies/mL</td>
<td>$150.00</td>
</tr>
<tr>
<td>16</td>
<td>HIV-1 RNA &lt;200 copies/mL</td>
<td>$150.00</td>
</tr>
<tr>
<td>20</td>
<td>HIV-1 RNA &lt;20 copies/mL</td>
<td>$150.00</td>
</tr>
</tbody>
</table>

**STEP 1: 24 wks**

**SOC**

(3 ARVs at least 2 active)

**STEP 2: 52 wks**

**SOC**

CROSS-OVER

- **RPV 25mg**
- **IM CAB LA (600 mg LD → 400 mg maint)**
- **+ IM RPV LA (900 mg LD → 600 mg maint)**
  (Q4wk) 

**STEP 3: 52 wks**

48 wks of IM CAB-LA + RPV-LA (cross over)

NOT randomized

**STEP 4: up to 52 weeks SOC “tail” for anyone receiving at least one dose of LA ARV**

Wk 128

$ $ $ $ $ $