“IM” Thinking About Using Long-Acting Injectables…

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Disclosures

Nothing to disclose
Objectives

• Consider potential pros and cons of switching to intramuscular (IM), long-acting cabotegravir-rilpivirine (LA CAB-RPV) for an individual with suppressed viral loads

• Review contraindications to LA CAB-RPV and factors that may predict worse outcomes

• Format for debate: case, then poll, followed by presentation of ”pro” side then “con” side, then repeat poll, then discuss
Case

• “L.A.” is a 50-year-old male diagnosed with HIV in 2005. He initially took EFV/FTC/TDF (Atripla) and did well until he experienced virologic failure in 2015 due to missed doses. He developed a K103N mutation and switched to DTG/ABC/3TC (Triumeq). He has some CVD risk factors, struggles with the large pill size, and misses some doses. Since switching to DTG/ABC/3TC he has had some low-level viremia but the HIV RNA has now been <50 copies/mL for over a year. He does not have hep B.
  - Other meds: lisinopril 20 mg daily, atorvastatin 10 mg
  - PMH: HTN, hyperlipidemia, obesity (BMI 32)
• **POLL**: Would you recommend this patient switch to LA-CAB/RPV to manage his HIV?

  A) Yes  
  B) No
Pro-Switch
Brian R. Wood, MD
Reasons to Vote **Yes** for IM CAB-RPV

- It works! Very effective with excellent long-term data
- It’s safe! Avoids all NRTI toxicity and serious AE’s rare
- It’s easy! Monthly dosing (every 2-month option coming)
- It’s preferred! People with HIV consistently prefer it
IM CAB-RPV Works!
Key Phase 3 Studies & Duration of Follow Up

• **Treatment-Naïve Individuals**
  FLAIR: IM CAB-RPV monthly vs. oral DTG-ABC-3TC daily: 124 weeks$^1$

• **Treatment-Experienced Individuals**
  ATLAS: switch to monthly IM CAB-RPV vs cont. 3-drug ART: 96 weeks$^2$
  ATLAS-2M: switch to IM CAB-RPV every 4 or 8 weeks: 96 weeks$^3$

• **Ongoing**
  MOCHA: LA CAB-RPV for children and adolescents
  SOLAR: switch to every 8 week IM CAB-RPV vs continue BIC-FTC-TAF
  LATITUDE: IM CAB-RPV vs oral ART with history of adherence issues

FLAIR: 96-Week Results
IM CAB-RPV Monthly vs Oral DTG-ABC-3TC for Initial ART


*HIV RNA ≥50 copies/mL at 96 weeks: n = 9 (3%) CAB-RPV, n = 9 (3%) DTG-ABC-3TC
*Resistance: 3 virologic failures with resistance in CAB-RPV arm (all from Russia, A1 virus)
Switch to IM CAB-RPV Monthly vs Continue Daily Oral ART

ATLAS Study: 48-Week Results

Weeks 48: Virologic Response by FDA Snapshot Analysis


*HIV RNA ≥50 copies/mL at 48 weeks: 1.6 % CAB-RPV, 1.0% 3-drug oral ART
*Resistance: 3 virologic failures with resistance in CAB-RPV arm (2 from Russia, A1 virus)
IM CAB-RPV: Safe and Well Tolerated!

• Injection site reactions common but mild & short-lived:
  - 89% grade 1, 11% grade 2
  - Median duration 3 days

• Adverse events leading to withdrawal quite rare:
  - FLAIR: n = 3 (1%) IM CAB-RPV, n = 4 (1%) DTG/ABC/3TC
  - ATLAS: withdrawal due to injection site reaction: n = 4 (1%)

• PLUS, no abacavir and no tenofovir!

• Greater improvements in treatment satisfaction and acceptability in FLAIR and ATLAS in LA arm compared to oral arm\textsuperscript{1}
  - ATLAS: all switch arm participants (100\%) surveyed preferred LA therapy to their previous daily oral regimen\textsuperscript{2}

• Reported benefits:\textsuperscript{3,4}
  - Convenience (e.g., no carrying pills when traveling)
  - Improved quality of life
  - Reduced stigma
  - Elimination of daily reminder of HIV, reduced emotional burden
  - Better for swallowing/GI difficulties
  - Reduced confidentiality/privacy concerns
  - 50\% felt it would improve adherence

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Now, for the opposing side…
Not so fast my friend....
David Hachey, PharmD
Three reasons *not* to switch

https://en.wikipedia.org/wiki/Neapolitan_ice_cream
Before Starting Therapy (Vanilla)

• Data - it is effective and safe…but for everyone?
  - Originally rejected by the FDA due to issues related to chemistry, manufacturing, and controls (CMC)
  - 34-40 yo white men with a normal BMI
    • Women of child-bearing potential and obesity??
  - Avoiding TAF/ABC
    • Discuss other oral options such as DTG/RPV and DTG/3TC
  - Drug interactions
    • Avoid several interactions with the injection, but strong inducers can lower levels of ART significantly
  - Excluding injection site reactions, still significantly higher rates of adverse drug reactions
    • Consider Torsade de Pointes in patients who may be on other medications (or be placed on these medications)

### Drug-Related Adverse Events and Injection Site Reactions (ISR)

<table>
<thead>
<tr>
<th>Drug-Related Adverse Event (AE)</th>
<th>IM CAB + RPV (n = 283)</th>
<th>DTG-ABC-3TC (n = 283)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>236 (83)</td>
<td>28 (10)</td>
</tr>
<tr>
<td>Any AE, excluding ISR</td>
<td>79 (28)</td>
<td>28 (10)</td>
</tr>
<tr>
<td>Grade 3 or 4 AE</td>
<td>14 (5)</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3 or 4 AE, excluding ISR</td>
<td>4 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Any injection site pain</td>
<td>227 (80)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Starting Therapy (Chocolate – most important)

Access

- The “Busy Badge”
  - Patients’ ability to get labs and see a provider every 6 months is challenging
  - Clinics are often understaffed, overworked, and don’t always have the personnel to manage coordinating who is on what and who needs injections when
  - Rurality of our patient population
  - Attending to these patients will take resources away from patients who really need nursing and provider attention

- Navigating Medication Acquisition
  - More paperwork, medication storage, prior authorizations, etc…

- CUSTOMIZE trial
  - Conducted by ViiV to assess perceived and actual barriers by healthcare teams
  - Respondents (N=26) indicated they felt LAI was acceptable, appropriate and feasible, but significant barriers exist

http://programme.aids2020.org/Abstract/Abstract/10530
### CUSTOMIZE Trial

<table>
<thead>
<tr>
<th>Perceived Barrier at Baseline N=26, %*</th>
<th>Actual Barrier at Month 4 N=24, %*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient ability to keep monthly appointments</td>
<td>80.8</td>
</tr>
<tr>
<td>Patient transportation for monthly appointments</td>
<td>76.9</td>
</tr>
<tr>
<td>Flagging/awareness of missed injection visits</td>
<td>73.1</td>
</tr>
<tr>
<td>Staff Resourcing for clinic flow</td>
<td>53.8</td>
</tr>
<tr>
<td>Rescheduling missed injections</td>
<td>50.0</td>
</tr>
<tr>
<td>Patients failing CAB+RPV LA due to missed doses/injection visits</td>
<td>50.0</td>
</tr>
<tr>
<td>Management of patients presenting to injection visits with other care needs</td>
<td>50.0</td>
</tr>
<tr>
<td>Patient injection pain/soreness</td>
<td>46.1</td>
</tr>
</tbody>
</table>
The leftovers (Strawberry)

• Does this create more ‘inequality’ in medicine??
  - “…this major advance in treating HIV infection will provide a new option for a select group of patients who currently have viral suppression while taking ART and represents the first step toward making less-frequent dosing of ART a reality.”
  - What about women of child-bearing potential, PWID, people dealing with housing instability, rural patients, relocating or traveling, etc…

• Switching back and forth from LAI to oral
  - This will become a reality based on changes in insurance, availability from pharmacies, non-adherence, and new meds
  - How do we handle virologic failures?

• Monitoring and follow up (see chocolate)
  - Most patients want to be seen less…not more often
Long-Acting ART: Be careful for what you wish for!

- Original denial from the FDA
- Other options for NRTI sparing regimens
- Drug interactions still exist
- Higher rates of side effects compared to oral therapy
- Increased staff/provider burden
- Inconvenience for patients to come to clinic monthly
- Driving inequality in health care
Review & Discussion
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Cabotegravir and Rilpivirine (Cabenuva) 
Extended Release Injectable Suspension: Reminders

• Indication
  - Replace ART regimen in persons with HIV RNA <50 copies/mL
  - Taking stable ART regimen
  - No history of treatment failure
  - No known or suspected resistance to cabotegravir or rilpivirine
  - No hepatitis B co-infection

• Additional considerations
  - Insurance coverage
  - Ability to attend clinic monthly
  - Drug-drug interactions
  - Other predictors of virologic failure: BMI >30, HIV subtype A6/A1 (associated with integrase polymorphism L74I)¹,²

Sources: Cabenuva Prescribing Information
**Cabotegravir and Rilpivirine (Cabenuva) Dosing Schedule**

**Oral Lead-In x 1 month (≥28 days)**
Cabotegravir 30 mg daily + Rilpivirine 25 mg daily

**Initiation Injections (x 1)**
Cabotegravir (600 mg): 3 mL IM + Rilpivirine (900 mg): 3 mL IM

**Continuation Injections (Monthly)**
Cabotegravir (400 mg): 2 mL IM + Rilpivirine (600 mg): 2 mL IM

*Administer injections at opposite gluteal sites (or at least 2 cm apart) and give both during the same visit.
*See prescribing guidelines or National HIV Curriculum for guidance on missed doses (planned or unplanned)

**Source:** Cabenuva Prescribing Information
Acknowledgment

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