Learning Objectives

1) Determine optimal timing for starting ARV therapy based on patient-specific factors and clinic resources.

2) Choose an optimal starting regimen for a newly diagnosed HIV-infected individual.

3) Support adherence and engagement in care for recently diagnosed individuals.
Case

• Nov 8, 2016 43yo male presented for PrEP
  – HIV and STD negative
  – Here with MSM HIV-negative partner in long-term relationship
  – Multiple partners
• 11/18/16 – gonorrhea positive
• 11/23/16 – 4th generation HIV Ag/Ab reactive, Ab differentiation indeterminate, VL qualitative positive – acute HIV infection
• 12/9/16 – pt in clinic for new diagnosis visit, had refilled Truvada week before – poorly adherent over past month
Goals of ARV Therapy

• Undetectable VL
  – Reduce transmission

• Restore immune system – for pts with low CD4 counts
  – Avoid HIV progression and OI

• Reduce inflammation – for patients at any CD4 count

• Reduce size of viral reservoir – for patients with acute HIV infection
Timing of ARV Initiation

Poll question –
Which of the following statements are most true for your work environment regarding starting ARV for newly diagnosed patients

1) ARV therapy is initiated at PCP appt when baseline labs (VL, CD4, genotype, HLAB5701, CMP) are available for review.
2) ARV therapy is initiated as soon as insurance and payer confirmed, whether labs back or not
3) ARV therapy is initiated as pt given HIV diagnosis, with starter packs while insurance/payer info being finalized
4) ARV therapy is initiated after intake visit, labs reviewed and patient confirms commitment to adherence (usually 2-4 visits with various team members)
5) I do not have experience starting ARV therapy in my work environment
Starting ARV therapy

• Current guidelines recommend starting ART regardless of CD4 count
  – DHHS guidelines updated 2012
  – WHO guidelines updated 2015

• Goals of this strategy
  – Reduce HIV transmission
  – Avoid HIV-related morbidity/mortality
  – Avoid adverse reactions to ART
  – Decrease inflammation
SF RAPID ART model

HIV+ Diagnosis
- Disclosure
- HIV education
- Counseling
- Referral
- Scheduling

1st Clinic Visit
- Registered
- Insurance
- Assess housing, substance use, mental health needs
- HIV education
- Counseling
- Labs

1st Primary Care Provider Visit
- Medical evaluation
- Assess preparedness

ART Start
- Prescription
- Pharmacy pick-up

ART Management
- Viral load monitoring
- Adherence
- Retention

RAPID Visit: ART Start
- Disclosure, counseling
- Registration
- Insurance
- Assess housing, substance use, mental health needs
- Labs
- HIV education
- Counseling
- Medical evaluation
- Assess preparedness
- ART dispensed
- Telephone follow-up

Primary Care Provider Visits: ART Management
- Viral load monitoring
- ART management
- Adherence
- Retention
5 day Starter Packs of ART

- Tenofovir DF/emtricitabine + dolutegravir (26/39)
- Elvitegravir/cobi/TDF/emtricitabine (7/39)
- Tenofovir DF/emtricitabine + darunavir/ritonavir (4/39)
- Tenofovir DF/emtricitabine + raltegravir (1/39)
- Abacavir/lamivudine/dolutegravir (1/39)
Poll Question

What are some reasons that NNRTI not part of starter packs in this study?

1) Some NNRTI not effective if CD4<200 and/or VL >100,000
2) NNRTI resistance more common in baseline genotypes than PI or INSTI
3) NNRTI have lower barrier for resistance if poorly adherent than PI or INSTI
4) NNRTI (particularly efavirenz) not as well tolerated as PI or INSTI
5) All of the above
Outcomes
# Time to Clinical Milestones

<table>
<thead>
<tr>
<th>Group</th>
<th>RAPID</th>
<th>Non-RAPID</th>
<th>Universal ART Era</th>
<th>CD4-Guided Era</th>
<th>Between-Group Comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients for whom ART recommended</td>
<td>All</td>
<td>All</td>
<td>All</td>
<td>CD4 &lt; 500</td>
<td></td>
</tr>
<tr>
<td>Received intervention</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>39</td>
<td>47</td>
<td>69</td>
<td>25</td>
<td>p*</td>
</tr>
<tr>
<td>Mean (range) time in days from referral to</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinic intake visit</td>
<td>1 (0–5)</td>
<td>10 (7–17)</td>
<td>13 (7–26)</td>
<td>9 (2–44)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Primary provider visit</td>
<td>14 (3–30)</td>
<td>26 (13–105)</td>
<td>31 (17–60)</td>
<td>30 (7–65)</td>
<td>0.13</td>
</tr>
<tr>
<td>ART prescription</td>
<td>1 (0–7)</td>
<td>22 (14–48)</td>
<td>37 (26–148)</td>
<td>128 (39–520)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Viral suppression &lt;200 copies per milliliter</td>
<td>56 (40–87)</td>
<td>79 (53–174)</td>
<td>132 (91–210)</td>
<td>218 (116–777)</td>
<td>0.009</td>
</tr>
<tr>
<td>Time in days from diagnosis to</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Referral to the clinic</td>
<td>6 (2–11)</td>
<td>11 (3–104)</td>
<td>14 (4–48)</td>
<td>33 (4–120)</td>
<td>0.004</td>
</tr>
<tr>
<td>Viral suppression &lt;200 copies per milliliter</td>
<td>65 (52–119)</td>
<td>170 (79–363)</td>
<td>190 (113–302)</td>
<td>580 (138–971)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Other notable findings

• More ART modifications in RAPID cohort vs non-RAPID
  – 2 patients due to rash, 10 patients due to simplification after HLAB5701 results avail
• Transfer of care to another HIV program similar for RAPID and non-RAPID cohorts (20.5% vs 23.4%)
• Lost to follow-up similar for both cohorts – occurring in 4/39 RAPID (10.3%) vs 7/47 non-RAPID (14.9%)
South Africa RapIT trial

Fig 1. Standard initiation of treatment and rapid initiation procedures and visit schedule.
Outcomes

- Initiated ≤ 90d & suppressed by 10 mo
  - STD 96/190 (51%)
  - Rapid 119/184 (64%)
- Initiated ≤ 90d & retained at 10 mo
  - STD 121/190 (64%)
  - Rapid 151/184 (81%)
- Crude rr 1.26 (1.05 – 1.50) and 1.27 (1.12 – 1.44) respectively
Case

- 43 yo 12/9/16 clinic visit 1 day after HIV diagnosis, RN & Intake, PharmD counseling sched for MD & PharmD f/u 12/13/16
- Has Truvada at home – PrEP regimen
- Insurance requires use of specialty pharmacy (Walgreens)
- Have starter packs of raltegravir in clinic (PEP) – Observed initiation
- Rx Genvoya sent to Walgreens
Case

- Pt no show to 12/13/16 appt
- Call to Walgreens – pt has not picked up Genvoya
- Pt returned call 12/16/16 – had taken 5 day starter pack, then no meds till started Genvoya that day.
- f/u HIV MD visit 12/23/16 – baseline CD4 516 VL24K
- f/u VL collected 1/17/17 – 72, 2/17/17 42
Case Timeline

11/23/16 HIV test to PCP – to pt and HIV clinic 12/8/16

12/9/16 RN/PharmD Intake and Rx

12/16/17 Genvoya Start

12/23/17 HIV MD visit

1/17/17 VL 72 – 56 days from HIV test
### Initial ARV Regimens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Details</th>
</tr>
</thead>
</table>
| **Tenofovir/emtricitabine + dolutegravir** | - Tenofovir alafenamide (Descovy) CrCl > 30ml/min  
- Few drug interactions  
- 2 pills once/day  
- Likely high genetic barrier to resistance |
| **Abacavir/lamivudine / dolutegravir** | - Need baseline HLAB5701 negative test  
- Few drug interactions  
- 1 pill once/day  
- Likely high genetic barrier to resistance |
| **Tenofovir/emtricitabine / elvitegravir/cobicistat** | - Tenofovir alafenamide (Genvoya) CrCl > 30ml/min  
- Significant drug interactions  
- 1 pill once/day with food  
- Moderate genetic barrier to resistance |
| **Tenofovir/emtricitabine + darunavir/boosted** | - Tenofovir Alafenamide (Descovy) CrCl >30ml/min  
- Significant drug interactions  
- Darunavir/cobicistat coformulated, can be 2 pills once/day  
- High genetic barrier to resistance |
| **Tenofovir/emtricitabine + raltegravir** | - Tenofovir alafenamide (Descovy) CrCl > 30ml/min  
- Few drug interactions  
- Twice daily dosing – raltegravir  
- Moderate genetic barrier to resistance |
Follow-Up ARV Initiation

• Phone follow-up calls 1 week after Rx
  – Confirm pharmacy dispensing
    • Co-Payments
    • Prior authorization
  – Respond to any questions
    • Auxiliary labeling/warning cards
  – Confirm adherence plan/tools
  – Confirm f/u labs and appointments
  – Manage side-effects – if any
Managing Side-Effects

• Nausea
  – Take ARV with food
    • Recommended for Stribild/Genvoya, rilpivirine and PI-based
  – Use Ginger to relieve symptoms
    • Can choose formulation per patient preferences
  – On occasion may need prescription antiemetics
    • Prochlorperazine, ondansetron, lorazepam
Follow-up after Initiation

• 2-8 weeks after initiation or change in ARV
  – VL
  – Complete metabolic panel
    • Asymptomatic bump in Scr from cobicistat and dolutegravir containing regimens

• Appointment to review lab work, assess adherence and strategies, side-effect monitoring and engagement in care strategies – often involves multiple team members
Initial Visit ARV start – 3-4 hour visit

RAPID Visit: ART Start
- Disclosure, counseling
- Registration
- Insurance
- Assess housing, substance use, mental health needs
- Labs
- HIV education
- Counseling
- Medical evaluation
- Assess preparedness
- ART dispensed
- Telephone follow-up
## Adherence Strategies

Table 1. Brief description of the 4 evidence-based HIV medication adherence strategies selected for translation into e-learning trainings for HIV providers.

<table>
<thead>
<tr>
<th>Strategy Name</th>
<th>Target population</th>
<th>Description</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart* (Helping Enhance Adherence to Antiretroviral Therapy)</td>
<td>ART-naive or changing ART regimen</td>
<td>Social support/problem-solving, individual/dyadic intervention delivered before and in the first 2 months after initiation of ART. A patient-identified support partner is required to attend at least 2 of the first 4 sessions. The intervention includes problem-solving activities to identify and address barriers. This information is used to develop an individualized adherence plan (IAP) for patient.</td>
<td>Five 1 1/2 to 2hr. sessions and 5 phone calls over 6 months</td>
</tr>
<tr>
<td>Partnership for Health - Medication Adherence</td>
<td>ART-experienced</td>
<td>Brief (3-5 minute), clinic-based individual-level, provider-administered intervention emphasizing the importance of the patient-provider relationship to promote patient’s healthful behavior. The intervention includes adherence messages delivered to the patient during routine medical visits and the use of posters and brochures conveying the partnership theme and ART adherence messages.</td>
<td>3 to 5 minute session at each clinic visit</td>
</tr>
<tr>
<td>Peer Support</td>
<td>ART-experienced or ART naive</td>
<td>Individual-and group-level intervention, where HIV-positive individuals, currently adherent to ART serve as peers, who provide medication-related social support through group meetings and weekly telephone calls to ART patients.</td>
<td>Six twice-monthly 1-hour group meetings and weekly phone calls over 3 months</td>
</tr>
<tr>
<td>SMART Couples Sharing Medical Adherence Responsibilities Together</td>
<td>HIV-discordant couples, with poor medication adherence in the HIV-positive partner</td>
<td>A couple-level intervention administered to discordant couples that addresses adherence to ART and safe sex behaviors within the couple dyad, fostering active support of both individuals.</td>
<td>Four 45-60 minute sessions over 5 weeks</td>
</tr>
</tbody>
</table>

* The first 2 sessions substitute as pre-medication and adherence counseling and are a routine part of HIV care.

The 4 adherence strategies can be delivered by a variety of HIV providers, including medical providers, licensed social workers, HIV case managers, health educators and/or peers.
Summary

• Models of rapid ARV start with HIV diagnosis demonstrate VL suppression more quickly.

• Some ARV regimens can be safely started prior to review of baseline labs

• Insurance, mental health, substance use, housing, HIV education and adherence support need to be addressed – can be done as ARV prescriptions started

• Workflows need to be developed for clinics to implement multidisciplinary intake visits, follow-up phone calls and adherence support, and starter packs ARV.
References


• Rosen S, et al Initiating Antiretroviral Therapy for HIV at a Patient’s First Clinic Visit: The RapIT Randomized Controlled Trial PLOS Medicine | DOI:10.1371/journal.pmed.1002015 May 10, 2016

• Guidelines for the use of antiretroviral agents in HIV-1 infected Adults and Adolescents, Department of Health and Human Services, updated July 14, 2016 https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/0

• Centers for Disease Control and Prevention (CDC) HIV Adherence Interventions https://effectiveinterventions.cdc.gov/en/HighImpactPrevention/BiomedicalInterventions/MedicationAdherence.aspx