The Transformation of HIV Care: From Specialty to Primary Care

- New HIV Treatment Paradigm
- Understand HIV treatment with current antiretrovirals.
- Identify standard Initial Treatment Antiretroviral Regimens.
- Identify essential components associated with successful control of HIV.
- Identify common triage issues and concerns
- List available resources.
Three Decades of Treatment Issues

- **1980’s**: AIDS described, PCP kills 90% of pts., clinicians develop skills in diagnosing, treating and preventing complications.

- **1990’s**: First effective treatments, patients respond, death rates drop.

- **2000’s**: New toxicities arise, resistance is critical, adherence issues emerge, limitations of therapy become apparent.

- **2007**: Second round of effective antiretroviral agents-integrase and CCR5 inhibitors.

- **2013**: Serious talk of “cure”.

- **2015**: PREP
Three Decades of Treatment Issues

- **1980’s**: AIDS described, PCP kills 90% of pts., clinicians develop skills in diagnosing, treating and preventing complications.

- **1990’s**: First effective treatments, patients respond, death rates drop.

- **2000’s**: New toxicities arise, resistance is critical, adherence issues emerge, limitations of therapy become apparent.

- **2007**: Second round of effective antiretroviral agents—integrase and CCR5 inhibitors.

- **2013**: Serious talk of “cure”.

- **2015**: PREP

In a little over 30 years, the treatment of HIV infection evolved from a complicated, progressive fatal illness handled by high volume providers to a chronic illness that can be managed in the primary care setting.
The New Treatment Paradigm of HIV Infection.

- Treat everyone, regardless of immune status or level of HIV-1 replication.
- Treating the newly diagnosed patient will involve simplified regimens utilizing co-formulated medications.
- With current treatment options, breakthrough viremia and the development of resistance should only occur in the setting of inadequate drug exposure.
- The newer antiretrovirals are no more toxic than many non-HIV medications.
- Drug interactions are less troublesome and usually easily predicted.
- Treatment prevents transmission.
Benefits of Treatment

- Treating people with AIDS greatly improves survival and quality of life.

- Treating people with advanced HIV (200-350 CD4 count) *may* delay disease progression and improve quality of life.

- Treating people with early HIV (>350 CD4 count) *may* delay progression of disease and preserve immune function.

- There is no “point of no return” for the untreated patient with AIDS.
Why Treat All HIV+ Patients?

- Medications are much less toxic, better tolerated.
- Treating HIV slows the inflammatory process.
- Treating HIV decreases risk of transmission.
Targets for HIV Inhibition

Entry Inhibitors
- T-20

Reverse Transcriptase Inhibitors
- ZDV, d4T, ddl, 3TC, FTC, ABC, TDF, EFV, NVP, DLV, TAF

Integrase Inhibitors
- T-20

Protease Inhibitors
- NFV, SQV, IDV, APV, r/ LPV, ATV, DAR

17 current drugs, more in development
# Current ARV Medications

## NRTI
- Abacavir (ABC)
- Didanosine (ddI)
- Emtricitabine (FTC)
- Lamivudine (3TC)
- Stavudine (d4T)
- Tenofovir DF (TDF)
- Tenofovir alafenamide (TAF)*
- Zidovudine (AZT, ZDV)

## NNRTI
- Delavirdine (DLV)
- Efavirenz (EFV)
- Etravirine (ETR)
- Nevirapine (NVP)
- Rilpivirine (RPV)

## PI
- Atazanavir (ATV)
- Darunavir (DRV)
- Fosamprenavir (FPV)
- Indinavir (IDV)
- Lopinavir (LPV)
- Nelfinavir (NFV)
- Saquinavir (SQV)
- Tipranavir (TPV)

## Fusion Inhibitor
- Enfuvirtide (ENF, T-20)

## CCR5 Antagonist
- Maraviroc (MVC)

## Pharmacokinetic (PK) Booster
- Ritonavir (RTV)
- Cobicistat (COBI)

## Integrase Inhibitor (INSTI)
- Dolutegravir (DTG)
- Elvitegravir (EVG)
- Raltegravir (RAL)

* TAF available only in coformulations:
  TAF/FTC, RPV/TAF/FTC, EVG/COBI/TAF/FTC
Current ARV Medications: Still in use.

<table>
<thead>
<tr>
<th>NRTI</th>
<th>PI</th>
<th>Fusion Inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir (ABC)</td>
<td>Atazanavir (ATV)</td>
<td>Enfuvirtide (ENF, T-20)</td>
</tr>
<tr>
<td>Didanosine (ddI)</td>
<td>Darunavir (DRV)</td>
<td></td>
</tr>
<tr>
<td>Emtricitabine (FTC)</td>
<td>Fosamprenavir (FPV)</td>
<td></td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>Indinavir (IDV)</td>
<td></td>
</tr>
<tr>
<td>Stavudine (d4T)</td>
<td>Lopinavir (LPV)</td>
<td></td>
</tr>
<tr>
<td>Tenofovir DF (TDF)</td>
<td>Nelfinavir (NFV)</td>
<td></td>
</tr>
<tr>
<td>Tenofovir alafenamide (TAF)*</td>
<td>Saquinavir (SQV)</td>
<td></td>
</tr>
<tr>
<td>Zidovudine (AZT, ZDV)</td>
<td>Tipranavir (TPV)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NNRTI</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Delavirdine (DLV)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efavirenz (EFV)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etravirine (ETR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nevirapine (NVP)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rilpivirine (RPV)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Integrase Inhibitor ( INSTI)**

Dolutegravir (DTG)
Elvitegravir (EVG)
Raltegravir (RAL)

**CCR5 Antagonist**

Maraviroc (MVC)

**Pharmacokinetic (PK) Booster**

Ritonavir (RTV)
Cobicistat (COBI)

* TAF available only in coformulations: TAF/FTC, RPV/TAF/FTC, EVG/COBI/TAF/FTC
Current ARV Medications: Initial regimens

**NRTI**
- Abacavir (ABC)
- Emtricitabine (FTC)
- Lamivudine (3TC)
- Tenofovir DF (TDF)
- Tenofovir alafenamide (TAF)*

**NNRTI**
- Efavirenz (EFV)
- Rilpivirine (RPV)

**PI**
- Atazanavir (ATV)
- Darunavir (DRV)
- Lopinavir (LPV)

**Integrase Inhibitor (INSTI)**
- Dolutegravir (DTG)
- Elvitegravir (EVG)
- Raltegravir (RAL)

**Fusion Inhibitor**

**CCR5 Antagonist**

**Pharmacokinetic (PK) Booster**
- Ritonavir (RTV)
- Cobicistat (COBI)

* TAF available only in coformulations: TAF/FTC, RPV/TAF/FTC, EVG/COBI/TAF/FTC
Initial ART Regimens: DHHS Categories

- **Recommended**
  - Easy to use
  - Durable virologic efficacy
  - Favorable tolerability and toxicity profiles

- **Alternative**
  - Effective but have potential disadvantages, limitations in certain patient populations, or less supporting data
  - May be the optimal regimen for individual patients

- **Other**
  - Reduced virologic activity; limited supporting data; or greater toxicities, higher pill burden, more drug interactions, or other limiting factors
Initial Treatment: Choosing Regimens

- 3 main categories:
  - 1 INSTI + 2 NRTIs
  - 1 PK-boosted PI + 2 NRTIs
  - 1 NNRTI + 2 NRTIs

- Combination of II, boosted PI, or NNRTI + 2 NRTIs is preferred for most patients

- NRTI pair should include 3TC or FTC

- Few clinical end points to guide choices: recommendations based mostly on rates of HIV RNA suppression and severity of adverse effects

- Advantages and disadvantages to each type of regimen

- Individualize regimen choice
### Initial Regimens: Recommended

**INSTI based**
- DTG/ABC/3TC; *(only if HLA-B*5701 negative)* (AI)
- DTG (QD) + TDF/FTC *(AI)* or TAF/FTC *(AII)*
- EVG/COBI/TAF/FTC
- EVG/COBI/TDF/FTC; *(only if pre-ART CrCl >70 mL/min)* (AI)
- RAL + TDF/FTC *(AI)* or TAF/FTC *(AII)*

**PI based**
- DRV/r (QD) + TDF/FTC *(AI)* or TAF/FTC *(AII)*

**Note:**
3TC can be used in place of FTC and vice versa; TDF: caution if renal insufficiency
Initial Regimens: Alternative

<table>
<thead>
<tr>
<th>NNRTI based</th>
<th>EFV/TDF/FTC (BI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EFV + TAF/FTC (BII)</td>
</tr>
<tr>
<td></td>
<td>RPV/TDF/FTC (BI) or RPV/TAF/FTC (BII); only if pre-ART HIV RNA &lt;100,000 copies/mL and CD4 &gt;200 cells/µL (BII)</td>
</tr>
<tr>
<td>PI based</td>
<td>(ATV/c or ATV/r) + TDF/FTC (BI) or TAF/FTC (BII)</td>
</tr>
<tr>
<td></td>
<td>(DRV/c or DRV/r) + ABC/3TC; only if HLA-B*5701 negative (BIII for DRV/c, BII for DRV/r)</td>
</tr>
<tr>
<td></td>
<td>DRV/c + TDF/FTC (BII) or TAF/FTC (BII)</td>
</tr>
</tbody>
</table>

Note:
3TC can be used in place of FTC and vice versa; TDF: caution if renal insufficiency
If HIV RNA <100,000 copies/mL and HLA-B*5701 negative:

- (ATV/c (CIII) or ATV/r (CII)) + ABC/3TC
- EFV + ABC/3TC (CI)
- RAL + ABC/3TC (CII)

Others to consider when TAF, TDF, or ABC cannot be used:

- DRV/r + RAL (BID) (CI) – only if HIV RNA <100,000 copies/mL and CD4 >200 cells/µL
- LPV/r + 3TC (CI)

Note: 3TC can be used in place of FTC and vice versa
Labs at Baseline

- General: CBC, CMP, UA
- Serologies: HAV, HBV, HCV, Toxoplasma,
- HIV specific: HIV-1 RNA, CD4 cell count/%, HLA B5701, genotype
- STI: syphilis test, GC/chlamydia screen, TB test
- Consider: lipid panel, targeted STI screening, HgbA1c, testosterone level for males, pap smear (vaginal and anal).
Resistance Tests

- **Genotype:**
  - Reports multiple known mutations associated with resistance *in vitro*; may be more reliable with new drugs.

- **Phenotype:**
  - Technically more complex, less available clinical data, may be helpful with highly resistant strain; takes into account compensatory changes.

- *Both tests reflect only the predominant strain at the time of specimen collection.*
**HIV GenoSURE™**

**GENOTYPING REPORT**

<table>
<thead>
<tr>
<th>Patient Information</th>
<th>Heating Information</th>
<th>Account Information</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Name / Initials:</strong></td>
<td><strong>LabCorp ID:</strong> 025-521-0084-1</td>
<td><strong>UPPER CUMBERLAND REGIONAL FAC</strong></td>
</tr>
<tr>
<td><strong>Patient ID:</strong></td>
<td><strong>Account Number:</strong> 418273999</td>
<td><strong>CDC</strong></td>
</tr>
<tr>
<td><strong>SSN:</strong></td>
<td><strong>LLG Client ID:</strong></td>
<td><strong>200 W. 10TH ST.,</strong></td>
</tr>
<tr>
<td><strong>Birth Date:</strong></td>
<td><strong>Collected:</strong> 01/25/2007</td>
<td><strong>COOKEVILLE,</strong></td>
</tr>
<tr>
<td><strong>Years / Months</strong></td>
<td><strong>Reported:</strong> 03/03/2007</td>
<td><strong>TN 38501</strong></td>
</tr>
<tr>
<td><strong>Age:</strong> 50 / 3</td>
<td></td>
<td><strong>TNF14</strong></td>
</tr>
<tr>
<td><strong>Visit:</strong></td>
<td></td>
<td><strong>Phone:</strong> (931) 526-7531</td>
</tr>
</tbody>
</table>

**Clinical Information:** SPEC@TQ ADDING@TQ 2225 OD-DBR418273999

**Clade / Subtype:** B

---

**Trade Name** | **Genetic Name** | **Interpretation** | **Associated Mutations** | **Comments**
---|---|---|---|---
**NNRTI** - Mutation Summary (31C, 190A)

- NNRTI: N/A
- Mutations at 333 are associated with ZDV/3TC dual resistance.

**NRTI** - Mutation Summary (32L, 674I, 701Q, 741I, 757T, 118S, 219F, 219Q, 2285)

- **Epi**
  - Lamivudine: **Sensitive**
  - L181, 333E
- **Foscarnet**
  - Zidovudine: **Resistant**
- **Didanosine**
  - Resistance Possible
  - L181, 215F, 219Q, 41L, 67N, 70R, 74L
- **Stavudine**
  - Resistance Possible
  - L181, 215F, 219Q, 41L, 67N, 70R, 75T
- **Abacavir**
  - Resistance Possible
  - L181, 215F, 219Q, 41L, 67N, 70R
- **Tenofovir**
  - Resistance Possible
  - L181, 215F, 219Q, 41L, 67N, 70R
- **Emtricitabine**
  - **Sensitive**


- **Lopinavir**
  - Inhibitory
  - 101, 46L, 47V, 50V, 53L, 54V, 60E, 62V, 63P, 71I, 89V, 90M
- **Indinavir**
  - Resistance
  - 101, 208, 33F, 46L, 50V, 53L, 54V, 60E, 62V, 71I, 89V, 90M
- **Saquinavir**
  - Resistance
  - 101, 46L, 54V, 50M
- **Ritonavir**
  - Resistance
  - 101, 208, 33F, 46L, 47V, 50V, 53L, 54V, 60E, 62V, 71I, 90M
- **Nelfinavir**
  - Resistance
  - 101, 208, 33F, 46L, 54V, 60E, 62V, 71I, 90M
- **Atazanavir**
  - Resistance
  - 101, 208, 33F, 46L, 47V, 50V, 53L, 54V, 60E, 62V, 71I, 89V, 90M
- **Tipranavir**
  - Resistance
- **Darunavir**
  - Resistance
  - 101, 46L, 50V, 53L, 54V, 60E, 62V, 71I, 89V, 90M

* A patient's response to therapy depends on multiple factors including the percentage of the patient's viral population that is resistant, drug pharmacokinetics, and medication compliance. Therefore, this test result should be interpreted in conjunction with the patient's antiretroviral treatment history, viral load count, and clinical status when making therapeutic decisions. This test may be unsuccessful if the plasma HIV RNA viral load is <1000 copies of virus per ml of plasma, measured with Roche AmpliCt Monitor assay (mp) (Roche Diagnostic Systems, Branchburg NJ).

* For NY State only. This test result is confidential HIV information and may not be disclosed except as outlined by NY State Law (art. 27F).

**Disclaimer:** This document contains private and confidential health information protected by state and federal law. This HIV Genotyping assay (GenoSURE) was developed and validated by LabCorp. Results from other test methods may provide different resistance interpretations.

---

**Technical Director:**
**Medical Director:**
Joseph Sebastian, Ph. D.
Janice J. Hessling, MD PhD

© 2000 Laboratory Corporation of America ® Holdings
Page 1 of 2
Printed: Saturday, March 3, 2007
## PHENOSENSE HIV Drug Resistance Assay

**ViroLogic Inc.**
Clinical Reference Laboratory
Patrick Joseph, M.D., Medical Director
345 Oyster Point Boulevard
South San Francisco, CA 94080
Tel:(800) 533-0587
Fax:(650) 815-0177

**LabCorp**
Laboratory Corporation of America-RTP
1912 Alexander Drive
Research Triangle Park, NC 27709
USA

### Patient Information
- **Client:** 00452
- **Project:** 08203
- **Referring Physician:** 02/03/2004 11:14
- **Date Collected:** 01/29/2004 00:01
- **Date Received:** 02/03/2004 11:14
- **Gender:** U
- **ViroLogic Accession #:** 04-104396
- **Date Reported:** 02/29/2004 09:11
- **ViroLogic Accession #:** 04-104396
- **Report Status:** FINAL
- **Mode:** OX

### Drug Resistance Analysis

#### NRTI

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Fold Change</th>
<th>Increasing</th>
<th>Drug Susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir</td>
<td>Ziagen</td>
<td>6.05</td>
<td>2.91</td>
<td>Increasing</td>
</tr>
<tr>
<td>Didanosine</td>
<td>Vridex</td>
<td>11.63</td>
<td>1.99</td>
<td>Increasing</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>Epivir</td>
<td>16.53</td>
<td>6.26</td>
<td>Increasing</td>
</tr>
<tr>
<td>Stavudine</td>
<td>Zentel</td>
<td>2.79</td>
<td>3.44</td>
<td>Increasing</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>Viread</td>
<td>0.827</td>
<td>1.98</td>
<td>Increasing</td>
</tr>
<tr>
<td>Zidovudine</td>
<td>Retrovir</td>
<td>0.277</td>
<td>6.64</td>
<td>Increasing</td>
</tr>
</tbody>
</table>

#### NRTI

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Fold Change</th>
<th>Increasing</th>
<th>Drug Susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delavirdine</td>
<td>Rescriptor</td>
<td>0.7569</td>
<td>18</td>
<td>Increasing</td>
</tr>
<tr>
<td>Efaviren</td>
<td>Sustiva</td>
<td>0.0064</td>
<td>5.21</td>
<td>Increasing</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>Viramune</td>
<td>&gt;20</td>
<td>MAX</td>
<td>Increasing</td>
</tr>
</tbody>
</table>

#### PIs

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Fold Change</th>
<th>Increasing</th>
<th>Drug Susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amprenavir</td>
<td>Agenerase</td>
<td>&gt;2</td>
<td>MAX</td>
<td>Increasing</td>
</tr>
<tr>
<td>Atazanavir</td>
<td>Reyataz</td>
<td>0.13492</td>
<td>81</td>
<td>Increasing</td>
</tr>
<tr>
<td>Indinavir</td>
<td>Crizalat</td>
<td>0.1645</td>
<td>21</td>
<td>Increasing</td>
</tr>
<tr>
<td>Lopinavir</td>
<td>Kaletra</td>
<td>&gt;1</td>
<td>MAX</td>
<td>Increasing</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>Viracept</td>
<td>1.0266</td>
<td>188</td>
<td>Increasing</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>Norvir</td>
<td>&gt;3</td>
<td>MAX</td>
<td>Increasing</td>
</tr>
<tr>
<td>Saquinavir</td>
<td>Fortovase</td>
<td>&gt;0.5</td>
<td>MAX</td>
<td>Increasing</td>
</tr>
</tbody>
</table>

### ASSESSMENT

**Drug**
- ABC
- ddC
- ddc
- d4T
- TDF
- TTV
- ZDV

**Sensitivity**
- Reduced Susceptibility
- Reduced Susceptibility

**Clinical Cutoff**
- Maximum Measurable
- Rolling Average

**Biological Assay Cutoff**
- Clinical cutoff derived from studies using IDV 800mg + RTV 200mg O2Lh.

**Replication Capacity (RC)**
- RC = 149%
- Range: 84% - 222%

**Virus Replication Capacity = 149%**

**Replication capacity (RC) indicates the ability of the virus to replicate in the absence of drug. Range represents 95% confidence interval around RC measurement. 100% median RC of wild type viruses.**
Initial Regimens: Simplification

- The patient has to be ready or nothing will work.
- If the patient is ready, has a WT genotype and has normal renal and liver function, the initial regimen will be one of the following:
  - Triumeq (1)
  - Genvoya (1)
  - Descovy + Tivicay (2)
  - Descovy + Prezcobix (2)
The patient has to be ready or nothing will work.

If the patient is ready and she has a WT genotype, is not coinfected with HBV and has normal renal and liver function, the initial regimen will be one of the following:

- Triumeq (1)
- Genvoya (1)
- Descovy + Tivicay (2)
- Descovy + Prezcoibix (2)

Generally potency of the initial regimen is not an issue. Co-morbidities, drug-drug interactions, formulary considerations may affect options.
Triumeq
(dolutegravir/abacavir/lamivudine)

- **PRO’s:**
  - Easy once a day one pill, non boosted regimen.
  - Well tolerated.
  - Minimal drug interactions.
  - Only three medications

- **CON’s:**
  - Patient must be HLA B5701 negative (abacavir component).
  - Does not treat HBV with two agents.
  - May have emerging psychiatric and weight gain concerns.
**Genvoya** (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamid)

- **PRO’s:**
  - Easy once a day, one pill, boosted regimen.
  - Well tolerated.
  - Treats HBV infection with two agents.
  - Slightly more durable NRTI backbone.

- **CON’s:**
  - Boosting leads to more drug interaction potential.
  - Integrase inhibitor may be less durable.
  - Four medications.
**Descovy** (emtricitabine/tenofovir alafenamid) + **Tivicay** (dolutegravir)

- **PRO’s**
  - Well tolerated.
  - Treats HBV infection with two agents.
  - Durable NRTI and INSTI agents.
  - Very small tablets.

- **CON’s**
  - Two pills daily.
  - Two copays.
  - May have dolutegravir side effects.
Descovy (emtricitabine/tenofovir alafenamid) + Prezcobix (darunavir/cobicistat)

- **PRO’s**
  - Relatively well tolerated.
  - Treats HBV with two agents.
  - Durable NRTI and PI agents.

- **Cons**
  - Two pills daily.
  - Two copays.
  - Four medications.
  - Increase drug reaction potential.
  - Very large pill.
Before Starting HAART

- The acutely ill: If an opportunistic infection, then waiting to treat OI may be reasonable.
- Elite controllers may be a special case. Studies are lacking to show treatment benefit.
- Adherence is key and factors known to affect adherence to treatment are critical in a time when most naïve patients can be treated successfully with one pill a day regimens.
Adherence

• Strict adherence to ART is key to virologic suppression, lower rates of resistance, better quality of life, improved survival, and decreased risk of HIV transmission
• Adherence also encompasses engagement and retention in care
• ART regimens have become much simpler for initial therapy, but suboptimal adherence is common
• Important to assess readiness for ART prior to initiating therapy, and to assess adherence at each clinic visit
Improving Adherence

• Provide education on HIV disease, treatment, and prevention
• Provide education on importance of adherence, and consequences of poor adherence
• Establish readiness to start therapy
• Individualize treatment, with patient involvement
Factors Associated with Adherence Failure

- Regimen complexity and pill burden
- Low literacy or numeracy level
- Younger age
- Some challenges of older age (e.g., polypharmacy, vision loss, cognitive impairment)
- Nondisclosure of HIV status
- Stigma
- Psychosocial stressors
- Active drug use or alcoholism
- Mental illness (especially depression)
- Cognitive impairment
- Lack of patient education
- Medication adverse effects
- Treatment fatigue
- Cost and insurance coverage issues
Factors Associated with Adherence Success

- Regimen simplicity, once-daily dosing
- Low pill burden
- Good tolerability
- Older age
- Multidisciplinary care (e.g. with case managers, social workers, pharmacists, psychiatric care providers)

- Directly observed therapy
- Trusting patient-provider relationship
- Use of motivational strategies
Predictors of Inadequate Adherence

- Age, race, sex, educational level, socioeconomic status, and a past history of alcoholism or drug use do NOT reliably predict suboptimal adherence.

- Higher socioeconomic status and education levels and lack of history of drug use do NOT reliably predict optimal adherence.
Once the prescription has been written.

- Formulary/Prior Authorization issues may arise.
- Initial GI side effects are common, usually resolve after 4-6 weeks and usually do not require treatment.
- Follow up call at 2 weeks to make sure everything is going well is very effective.
- Labs should be obtained in 4-6 weeks after starting HAART. After that every 3 month lab monitoring which can be spread out to every 6 months if stable.
- Monitoring labs include CBC, CMP, HIV-1 RNA and CD4 count/%
- If a patient has detectable virus after obtaining virologic control, then a call should be made to determine adherence, follow up labs with genotyping as well.
Initial Treatment of the Patient with AIDS

- The period after starting HAART in an immune compromised patient is more challenging:
  - Side effects may be more frequent or severe
  - The patient is at risk for new AIDS related diagnoses until immune reconstitution occurs.
  - The patient is at risk for IRIS
Initial Treatment of the Patient with AIDS

- The period after starting HAART in an immune-compromised patient is more challenging:
  - Side effects may be more frequent or severe
  - The patient is at risk for new AIDS-related diagnoses until immune reconstitution occurs
  - The patient is at risk for IRIS

The term "immune reconstitution inflammatory syndrome" (IRIS) describes a collection of inflammatory disorders associated with paradoxical worsening of preexisting infectious processes following the initiation of highly active antiretroviral therapy (HAART) in HIV-infected individuals.
### General management recommendations for specific IRIS-related syndromes*

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Most common clinical manifestations</th>
<th>Management recommendations</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>General IRIS</td>
<td></td>
<td>Consider concurrent unmasked infection, persistent active infection, antimicrobial resistance, adverse drug reaction, and medicine nonadherence.</td>
<td>Generally self-limited</td>
</tr>
<tr>
<td>M. tuberculosis</td>
<td>Pneumonia</td>
<td>Consider the possibility of multidrug resistant TB. Incise and drain the initial episode of adenitis for diagnostic purposes and symptomatic relief. For moderate severity or CNS involvement, prednisone (1.0 mg/kg, up to 80mg daily) or dexamethasone 8-16 mg/day divided in twice daily doses and tapered after 1-2 months. Use as adjunct to anti-tuberculous therapy. Continue HAART.</td>
<td>Generally self-limited</td>
</tr>
<tr>
<td>M. avium complex</td>
<td>Lymphadenitis</td>
<td>Indicision and drainage or aspiration for the initial episode of adenitis. If illness is severe, adjunct corticosteroids (as above) in addition to standard anti-MAC therapy. Continue HAART.</td>
<td>Self-limited in the vast majority</td>
</tr>
<tr>
<td>Cryptococcus spp.</td>
<td>Meningoencephalitis</td>
<td>Continue antifungal therapy. Adjunct corticosteroids, if illness is severe or not self-limited. Continue HAART.</td>
<td>Generally self-limited</td>
</tr>
<tr>
<td>Pneumocystis carinii</td>
<td>Pneumonia</td>
<td>Standard course of anti-Pneumocystis antimicrobial therapy. Adjunct corticosteroids. Continue HAART.</td>
<td>Generally self-limited when corticosteroid therapy is used</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>Uveitis/vitritis</td>
<td>Continue HAART&lt;sup&gt;1&lt;/sup&gt;. Anti-CMV antiviral therapy if concurrent CMV retinitis is present. Topical, intracocular, or systemic corticosteroids in conjunction with close ophthalmologic follow-up&lt;sup&gt;3&lt;/sup&gt;. Vitreectomy may be needed if vitreomacular traction occurs.</td>
<td>Generally good, but long-term sight-threatening complications may occur</td>
</tr>
</tbody>
</table>

* Based on published clinical experience, but needs to be proven in controlled clinical trials.

<i>Consider delaying HAART therapy for 1-2 months if not already begun.</i>

<i>Consider temporarily interrupting HAART for 1-3 months if eye, neural, liver, or other organ involvement is particularly severe, progressive, and/or steroid refractory.</i>

:o Can alternatively use topical or systemic non-steroidal anti-inflammatory agents.
## General management recommendations for IRIS-related syndromes, continued*

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Most common clinical manifestations</th>
<th>Management recommendations</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>JC virus</td>
<td>Progressive multifocal leukoencephalopathy with inflammatory features</td>
<td>Continue HAART in most cases. Corticosteroids.</td>
<td>Often self-limited, but chronic neurologic sequelae and fatal cases may occur.</td>
</tr>
<tr>
<td>HSV, VZV</td>
<td>Perianal herpes. Localized zoster</td>
<td>Continue HAART. Oral acyclovir or famciclovir for 7-14 days.</td>
<td>Self-limited in the vast majority</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Hepatitis</td>
<td>Consider direct drug hepatotoxicity (eg, protease inhibitor). Continue or interrupt HAART.</td>
<td>Often self-limited, but progressive cirrhosis may occur, esp with low functional hepatic reserve.</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>Hepatitis</td>
<td>Consider direct drug hepatotoxicity (eg, protease inhibitor). Continue or interrupt HAART.</td>
<td>Same as above.</td>
</tr>
<tr>
<td>Parvovirus B19</td>
<td>Fever, anemia. Encephalitis</td>
<td>Intravenous immunoglobulin (IVIG). Continue or interrupt HAART.</td>
<td>Usually self-limited.</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Pulmonary</td>
<td>Corticosteroids. Continue HAART.</td>
<td></td>
</tr>
<tr>
<td>Autoimmune thyroiditis</td>
<td>Thyrotoxicosis.</td>
<td>Anti-thyroid drugs, beta-blockers, and/or thyroid ablation. Continue HAART.</td>
<td></td>
</tr>
</tbody>
</table>

* Based on published clinical experience, but needs to be proven in controlled clinical trials.

Δ Consider temporarily interrupting HAART for 1-3 months if eye, neural, liver, or other organ involvement is particularly severe, progressive, and/or steroid refractory.
Sharon

- 26 year old female call center worker who tests positive after being notified by the HD of possible sexual exposure.
  - No significant past medical history.
  - No substance abuse or mental health issues.
  - Single, not in a stable relationship.
  - CD4 count is 643/43%
  - HIV 1 RNA is 343,280 copies/ml
Sharon

- Given what you have been told, which of the following first line regimens would you select for this patient?
  
  **Triumeq** (dolutegravir/abacavir/lamivudine)
  
  **Genvoya** (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamid)
  
  **Descovy** (emtricitabine/tenofovir alafenamid) + **Tivicay** (dolutegravir)
  
  **Descovy** (emtricitabine/tenofovir alafenamid) + **Prezcobix**
    
    (darunavir/cobicistat)
Sharon revisited

- Sharon has been on Triumeq for 4 months and is doing well. Last CD4 count was 965/34% and HIV-1 RNA is less than 20 copies/ml.
  - She calls to let you know she has gained about 22 pounds and was seen by a holistic healer who has prescribed several costly supplements. She wants to make sure it is ok.
    - Any concerns or questions?
    - How would you handle it?
Chad

- 48 year old male who works as a traveling auditor tests positive for HIV as part of a syphilis contact follow up.
  - PMH is significant for Type II DM, HTN and recent ACS.
  - Medications include ACEI, metformin, ASA, simvastatin and metoprolol.
  - History of intermittent methamphetamine abuse and binge drinking.
  - He is divorced, has multiple MSM contacts on the road.
  - CD4 count is 283/14%, HIV-1 RNA is 22,524 copies/ml
Given what you have been told, which of the following first line regimens would you select for this patient?

- **Triumeq** (dolutegravir/abacavir/lamivudine)
- **Genvoya** (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamid)
- **Descovy** (emtricitabine/tenofovir alafenamid) + **Tivicay** (dolutegravir)
- **Descovy** (emtricitabine/tenofovir alafenamid) + **Prezcobix** (darunavir/cobicistat)
Chad revisited

- Chad calls several months later. He has been doing well on Genvoya. His CD4 count is now 568/26% and HIV-1 RNA is less than 20 copies/ml.
  - He has called because he was seen in a walk in clinic for cold symptoms and was treated with a “Z-Pack” and steroid taper. He was called by the clinic nurse three days later because his routine labs showed “kidney problems”.
  - You bring him in and repeat labs reveal a creatinine of 2.2 mg/dl (baseline was 0.8 mg/dl).

- What do you do?
William

- 51 year old male hardwood floor installer tested positive during 28 day rehab stay for crack cocaine.
  - PMH significant for HBV infection, HTN, CAD.
  - Medications include lisinopril, Xeralto (Rivaroxaban), zolpidem, HCTZ, sertraline.
- He is divorced, not in a relationship at present.
- History of polysubstance abuse, depressive disorder.
- CD4 count is 208/16%, HIV-1 RNA is 640,233 copies/ml.
Given what you have been told, which of the following first line regimens would you select for this patient?

- **Triumeq** (dolutegravir/abacavir/lamivudine)
- **Genvoya** (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamid)
- **Descovy** (emtricitabine/tenofovir alafenamid) + **Tivicay** (dolutegravir)
- **Descovy** (emtricitabine/tenofovir alafenamid) + **Prezcobix** (darunavir/cobicistat)
William revisited

- William calls after about 9 weeks. He states that he feels terrible with nausea, vomiting, abdominal pain. He reports losing 11 pounds and had stopped meds about 3 weeks ago.

  - What are your major concerns?
  - How would you handle it?
When to contact expert help in a newly treated patient.

- Severe intolerance or adverse effects.
  - Nausea/vomiting, rash, elevated LFT’s or creatinine.
- Treatment failure
  - Issues may arise regarding restarting same medications or reconsidering.
- New medication interaction issues.
  - New specialty medication added without consideration of drug interactions.
- New co-morbidities.
  - New co-morbidity that might make current HAART regimen less attractive.
Getting Expert Help When Needed

- The Southeast has several resources for expert help:
  - Participation in the VCCC ART conference is available online.
  - The AETC and the Southeast AETC has web based trainings, slide sets and access to PREP and Treatment hotlines.
  - Staff at the VCCC is always willing to help: 615 875 5111 (office); 615 587 3175 (cell).
AIDS 1985
One Patient’s Experience

- 322 IV insertions
- 14 hospital admissions
- 11 months of hospital stay
- 60 phlebotomies
- 32 chest x-rays
- 5 CT scans of head
- 3 abdominal ct scans
- 6 bronchoscopies
- 8 intubations
- 4 lumbar punctures
- 3 bone marrows
- 5 cycles of chemo
- 2 lymph node bx
Useful HIV Websites

www.vanderbilthealth.com/vccc
www.aidsinfonet.org
www.aidsetc.org
www.hivatis.org (DHHS, USPHS/IDSA Guidelines)
www.cdc.gov/nchstp/hiv_aids.htm
www.hiv-web.lanl.gov (Resistance mutations)
www.niaid.nih.gov
www.AIDS.medscape.com
www.hopkins-aids.edu
www.iapac.org
www.igm.gov
www.centerwatch.com
www.ucsf.edu/medical
www.virology.net