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HIV treatment failure; ART toxicity & complications

Morgan Younkin

Lawrence Family Medicine Residency

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HIV treatment failure; ART toxicity & complications
Overall Outline

5 session, 2 hours each

1. HIV & ART overview
   ◦ History, Epidemiology, transmission/risk, staging
   ◦ Med Class Overview, ART initiation

2. Treatment monitoring & Failure
   ◦ 2nd & 3rd line ART, toxicity/complications, monitoring
   ◦ Prevention

3. Opportunistic Infections & Hepatitis B
   ◦ OIs, ART considerations, Prophylaxis
   ◦ HBV dx, tx, surveillance, & HIV-HBV co-infection

4. Special Populations:
   ◦ Pregnancy, antenatal & intrapartum, infant care & pediatric

5. HIV/HBV Case-Based Application
   1. Case Application
   2. Wrap-up/review, miscellaneous items
Source Materials

Liberia Integrated Guidelines for Prevention, Testing, Care, and Treatment of HIV and AIDS
- 5th edition, August 2019

WHO HIV Diagnosis, Treatment, and Opportunistic Infection Guidelines
- 2016, 2018 ART update

WHO Hepatitis B treatment guidelines (2015)

Reference Materials


Outline

Mechanism of Resistance & defining terms

Resistance Pathways for each ART class

Treatment failure: 2\textsuperscript{nd} & 3\textsuperscript{rd} line ART

ART adverse effects

ART drug-drug interactions
Case

34yo on EFV/TDF/3TC. She has lost 20 pounds in 6 months with diarrhea.

She discloses that she generally takes her meds 3-4 days a week. She misses medications on days when she travels to a nearby village to sell goods and leaves early in the morning.

Next step?

What findings and factors might prompt concern for resistance?
Foundations of Treatment Failure

ART = Selective Pressure Determines Viral Fitness

Viral Population
- The most fit virus prevails at any given time point
- Once resistance is selected it will remain in the population

Drug + Replicating virus → Resistance

Wild-type drug sensitive HIV in an antiretroviral-naive person
- No drug pressure

Resistance emerging in a person on antiretroviral drug pressure

Current resistance assays have difficulty detecting resistant variants if they make up less than 20% of the circulating viral population.

No drug pressure in a person with resistant strains

Resistance re-emerges when drug pressure is re-applied

Pre-Treatment  Initial Response  Adherence Problems

Viral reservoirs
- Wild Type HIV
- Resistant HIV
How resistance happens:

- Poor adherence
- Insufficient drug level
- Viral replication in the presence of drug
- Resistant virus
- Treatment failure

Factors:
- Social/personal issues
- Regimen issues
- Toxicities
- Poor adherence
- Wrong dose
- Host genetics
- Poor absorption
- Rapid clearance
- Poor activation
- Drug interactions
- Suboptimal potency

Transmission:
- ~10% in United States & Western Europe
Basic Resistance Model

Theoretical Zone of Selective Pressure

Probability of Resistance

ART Concentration

IC₅₀  IC₉₀  IC₉₉
Virologic Suppression

Incomplete Virologic Response

Viral Blip

Antiretroviral Therapy Started

ART Started

Virologic Rebound

Low Level Viremia

HIV RNA (copies/mL)

Weeks
Terms

Successful ART

Potential Treatment Failure

Confirmed Treatment Failure

VL not detected

Routine VL detectable (even if < 1,000)

Targeted or repeat VL > 1,000

AND

Patient on NNRTI-based regimen*

AND

Good adherence for 3 months prior

*genotype for INSTI- or PI-based
Genetic Barrier to Resistance

**Genetic Barrier**
Number of mutations needed to confer resistance

- **Low Trough**: Non-Boosted PI
  - Small Change per Mutation
  - But Low Drug Levels
- **High Trough**: NNRTI
  - High Drug Levels
  - Large Change per Mutation
- **Boosted PI**: Small Change per Mutation
  - And High Drug Levels

Increasing Number of Mutations

Kuritzkes et al 2003; Bositis 2019
Cross-resistance

Resistance to 1 agent in a class → resistance to other agents in the same class

First generation NNRTI & INSTI
- High level of cross-resistance

NRTI
- Varies
  - emtricitabine (FTC) & lamivudine (3TC) = complete cross-resistance

PI & second-generation NNRTI
- Cumulative progressive resistance mutations expands cross-resistance
Adherence

“What challenges have you had taking your ARV?”

“What days / times are you most likely to forget your ARV?”

“Everyone has difficulty taking meds every day. When was the last time you were not able to take your ARV, and how many times in the past week, month were you unable?”

Root cause: there is always a reason (or reasons)
- Stigma & disclosure
- Socio-economic barrier
- Transportation & Work
- Psychological
- Misunderstanding
- Side effects

Goal: >95% adherence

Goal: to help the patient
- No policing
- Encourage transparency

Practical Strategies
- Join with daily routines (meal, cleaning)
- Cell phone alarm
- Take meds with another person
- Keep a med diary
Intensive Adherence Counseling (IAC)

for any sign of poor adherence
for any detectable Viral Load (even is <1k)

Patient & Treatment Supporter

Education on ART, adherence, monitoring, failure, & resistance

Identify Specifics
- Travel, Work, Education
- Stigma, Privacy, Domestic Difficulties
- Substance Use
- Mental Health / Depression

Action Plan
- Specific
- Written on Patient Card
- Monthly appointments
  - Pill Counts
  - Action Plan review
- Viral Load in 3mo

Stopping ART considered if:
- Chronic poor adherence
- IAC counseling completed
- Shared decision making
Mutation Nomenclature

Wild-type amino acid → codon position → mutant amino acid

103 = codon (amino acid position)

K = Wild-type amino acid
N = Mutant amino acid

Reverse Transcriptase
NRTI Resistance Mechanisms

**Discrimination**
[decreased incorporation of NRTI into DNA strand]

**Excision**
[removal of NRTI from the DNA strand]
NRTI Resistance Pathways

**3TC**

- **M184I > M184V**
  - Reverses TAM-associated resistance to: TDF & AZT
  - Resistance to: 3TC, FTC
  - Low level resistance to: ABC

**AZT or d4T**

- TAM [thymidine analogue mutations]
  - Cumulative Cross-Resistance
  - Class-wide

**TDF or ABC**

- **K65R**
  - Resistance to: TDF, 3TC, ABC
  - ^ Susceptibility: AZT

---

TDF – tenofovir
3TC – lamivudine
ABC – abacavir
AZT – zidovudine

Decreases viral fitness

Co-occurrence worsens ABC + 3TC resistance

*Common in monotherapy
Temporal Sequence of NRTI mutations

- **AZT/3TC**: M184V → TAMs
- **ABC/3TC**: M184V → K65R
- **TDF/3TC**: M184V → K65R

Time
Empiric NRTI Resistance

Monotherapy to TDF or 3TC (or PrEP with TDF/3TC)
- Likely M184V, possible K65R
- Assume resistance to TDF, 3TC, & ABC
- Unlikely TAM = use AZT

Confirmed virological failure
- Assume resistance to NRTIs in regimen & switch:
  - If on TDF or ABC -> AZT
  - If on AZT -> TDF/3TC

May always continue 3TC after failure
- Inducing M184V decreases viral fitness

Assume M184V / K65R
Resistance: 3TC, TDF, likely ABC

Assume Susceptibility to: AZT
*may give 3TC (AZT/3TC combo) or TDF
to select for M184V/K65R to ^ AZT susceptibility

Assume Resistance Class-Wide
due to TAM

May give: TDF/3TC to induce
M184V -> ^ TDF susceptibility
**NNRTI Resistance Mechanisms**

**Low Barrier** to resistance
- **Pre-existing** mutations found in all ART-naïve patients are selected **quickly** – within 1 - 4 weeks!
- All NNRTIs bind in a **similar location**

**HIV-2** – intrinsically resistant to all NNRTI

- **Reduced Access** to NNRTI-binding pocket
- **Altered Interaction** with NNRTI-binding pocket
NNRTI Resistance Pathways & Empiric Approach

EFV – efavirenz
NVP – nevirapine

EFV

K103N

Resistance to EFV + NVP

Highly fit virus

NVP

Y181C

Resistance to NVP

Resistance to EFV quickly develops

No impact on viral fitness

Hypersensitive to AZT

failure

EFV or NVP

Class-wide Resistance
Stop NNRTIs
PI Resistance Mechanisms

Barrier to resistance is *HIGH*

1. darunavir / ritonavir
2. lopinavir / ritonavir
3. atazanavir / ritonavir

Multiple mutations generally needed for resistance
- Major – cause resistance
  - Many have cross-resistance
  - Often decrease viral fitness
- Minor – do not affect susceptibility but may enhance viral replicative capacity

Multiple Mutations
Generally required to alter enzymatic activity
Viral Resistance Mutations are Rare – Adherence / absorption predominates

Suspected Treatment Failure on Boosted PI → Intensive Adherence Counseling

Virologic Failure more likely if prior treatment experience with a different PI

Important to confirmed good adherence prior to viral load!
PI Resistance Pathways

**ATV/r**
- **I50L**
- Resistance to ATV
- ^Susceptibility^ to other PIs

**LPV/r**
- Multiple mutations
- Significant cross-resistance to ATV

**DRV + r**
- **I50V**
- **Major Resistance** to DRV/r
- Minor Resistance to LPV
- ^Susceptibility^ to ATV

**LPV/r** – lopinavir / ritonavir
**ATV/r** – atazanavir / ritonavir
**DRV + r** – darunavir + ritonavir
Empiric PI Resistance

FAIL: ATV/r

Assume I50L
*may trial LPV/r or DRV/r AND/OR INSTI

Ensure good adherence

FAIL: LPV/r

Assume ATV/r resistance
May trial DRV + r AND/OR INSTI

Ensure good adherence

FAIL: DRV + r

Assume I50V (LPV/r & DRV/r resistance)
Will need INSTI, ?ATV/r if no prior tx history

Genotype
INSTI Resistance Mechanism

**High Barrier to Resistance**: Viral Resistance Mutations are Rare – Adherence / absorption predominates

- DTG Highest barrier to resistance
  - Little cross-resistance to earlier INSTIs (elvitegravir [EVG] & raltegravir [RAL])
  - Very little phenotypic resistance seen even in patients on failing regimens

Time on regimen $\Rightarrow$ likelihood of resistance
INSTI Resistance Pathways & Empiric Resistance

If documented virologic failure:
ADD Boosted PI (DRV + r)
Change “Base”

Ensure good adherence

Genotype

DTG failure
Back to our case...

To refresh: missing about 50% of doses on EFV/TDF/FTC with diarrhea and weight loss over 6mo

- Next step?
- Then?
- Then?
Treatment Monitoring & Follow-up

**When to do VL**

- **Any of the following:**
  - Significant unintended weight loss
  - Failure to thrive
  - New or worsening HIV-related disease (suspected or confirmed)

**Result and Action**

<table>
<thead>
<tr>
<th>VL Result</th>
<th>Interpretation</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any detectable VL</td>
<td>Potential Failure</td>
<td>Continued ART</td>
</tr>
<tr>
<td>Below detection limit</td>
<td>Successful ART</td>
<td>Intensive Adh. Support</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>VL Result (copies / ml)</th>
<th>Current Regimen</th>
<th>Interpretation</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below detection limit (DL)</td>
<td>Successful ART</td>
<td>Intensive Adh. Support</td>
<td>Continue current regimen</td>
</tr>
<tr>
<td>Above DL but &lt;1000</td>
<td>Potential Failure</td>
<td>Genotype testing</td>
<td>Continue current regimen</td>
</tr>
<tr>
<td>1000+</td>
<td>Poor adherence or failure</td>
<td>Intensive Adh. Support</td>
<td>Continue current regimen</td>
</tr>
<tr>
<td>0 - 6</td>
<td>Continued Failure</td>
<td>Start 2nd Line</td>
<td>Genotype testing</td>
</tr>
<tr>
<td>7 - 15</td>
<td>Poor adherence or failure</td>
<td>Intensive Adh. Support</td>
<td>Continue current regimen</td>
</tr>
</tbody>
</table>

**Notes:**
- NNRTI-based
- INSTI-based
- Switch to 2nd line (PI or INSTI)
- Boosted PI- or INSTI-based
- Poor adherence OR failure
- Genotype
- VL >1,000 while adherent to ART
- Wait
- Routine scheduled

**Decision Tree:**
- Less than 6 Months
- Between Milestones
- Around milestone (-1 to +12 months)
- Ever had VL
- Ever
- Never
- Well
- Not Well *
- Targeted/Follow-up VL
Definitions (review)

Successful ART

Potential Treatment Failure

Confirmed Treatment Failure

VL not detected

Routine VL detectable (even if < 1,000)

Targeted or repeat VL > 1,000
AND
Patient on NNRTI-based regimen*
AND
Good adherence for 3 months prior
*genotype for INSTI- or PI-based
First Line ART

**START**

<table>
<thead>
<tr>
<th>Core</th>
<th>Backbone</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTG</td>
<td>TDF / 3TC</td>
</tr>
<tr>
<td>EFV</td>
<td>TDF / 3TC</td>
</tr>
<tr>
<td>NVP</td>
<td>AZT / 3TC</td>
</tr>
</tbody>
</table>

- Men 30kg
- Women 45yo +
- Women of childbearing potential "B+
- Patients < 30kg

**Not for START**

<table>
<thead>
<tr>
<th>Core</th>
<th>Backbone</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTG</td>
<td>AZT / 3TC</td>
</tr>
<tr>
<td>EFV</td>
<td>ABC / 3TC</td>
</tr>
<tr>
<td>NVP</td>
<td>TDF / 3TC</td>
</tr>
</tbody>
</table>

+ ABC / 3TC
We have determined that our patient has a failed EFV/TDF/FTC regimen.

- What is your next step?
### 2nd line ART

<table>
<thead>
<tr>
<th>Core</th>
<th>Backbone</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATV/r</td>
<td>TDF / 3TC</td>
</tr>
<tr>
<td></td>
<td>AZT / 3TC</td>
</tr>
</tbody>
</table>

### Not for START*

<table>
<thead>
<tr>
<th>Core</th>
<th>Backbone</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPV/r</td>
<td>TDF / 3TC</td>
</tr>
<tr>
<td></td>
<td>ABC / 3TC</td>
</tr>
<tr>
<td></td>
<td>AZT / 3TC</td>
</tr>
</tbody>
</table>

*1st line START for < 3yo IF extra support

ATV/r
LPV/r
TDF
AZT
ABC
3TC
Case (cont)

Fast forward 3 years.
- Our patient who was switched to ATV/r/AZT/3TC now presents with a routine VL of 2,350

Next step?
Then?
Then?
### 3rd line ART

#### 2 Core Agents

<table>
<thead>
<tr>
<th>Combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRV + r</td>
</tr>
</tbody>
</table>

*DTG is BID if INSTI resistance

#### Backbone

<table>
<thead>
<tr>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF / 3TC</td>
</tr>
<tr>
<td>ABC / 3TC</td>
</tr>
<tr>
<td>AZT / 3TC</td>
</tr>
</tbody>
</table>

#### Assumptions

- Assumes likely resistance to at least 2 prior agents
  - Assumes failure to prior treatment with core of:
    - ATV/r | LPV/r | DTG
  - For likely NRTI resistance, “flip” the backbone (or follow genotype)
    - If failed on:
      - ABC or TDF → AZT
      - AZT → TDF

- Switch to:
Our patient now on DRV/r/DTG/AZT/3TC presents with asymptomatic viral load of 1,230

- What do you think is going on here?
- What do you do?
Genotype Overview

Obtain for failure evaluation while on PI- or INSTI-based regimens
  ◦ **Rationale**: to differentiate resistance virus from poor adherence / low drug levels

**When to obtain a genotype**: while the patient is **taking failing ART with detectable virus**!
  ◦ Genotyping is sensitive to resistance mutations *only* if they are present in a minimum of ~20% of circulating virus at the time of the test
  ◦ In the **selective** presence of ART → **mutant virus** is advantaged and present
  ◦ In the **absence** of ART → **wild-type virus** is generally most fit and predominates

A patient with history concerning for prior virologic failure due to resistance is currently off ART.
  ◦ What are your next steps?
Obtaining & interpreting a Genotype

PCR -> averaged genetic sequence -> compared to wild-type

Stanford Resistance Database
Switching regimen (Table 10)

- Contraindication to regimen
- Immediate significant adverse effect
- Troubling but tolerable side effect
- Failure to improve after 2 mo of continued ART & symptom management
- Contraindication or adverse effect

Switch to Alternative 1
Switch to Alternative 2
Initial Treatment Failure (go to Alt 1)

NNRTI-based

Confirmed virologic failure

ATV/r

+ 

AZT / 3TC  
or

TDF / 3TC  
If prior TDF/3TC

If prior AZT/3TC

or ABC/3TC

ATV/r-based

Confirmed virologic failure

or

LPV/r-based

Confirmed virologic failure

genotype

DRV + r

+ 

DTG

AZT / 3TC  
or

TDF / 3TC  
If prior TDF/3TC

If prior AZT/3TC

or ABC/3TC

DTG-based

Confirmed virologic failure

genotype

ATV/r

+ 

AZT / 3TC  
or

TDF / 3TC  
If prior TDF/3TC

If prior AZT/3TC

or ABC/3TC
2nd line follow-up

Initial 6 months:
◦ Q 4 weekly visits

If stable, transition to Q 8 weekly visits

** EFV or NVP **

** Remember the “tail” if switching off these! **

EFV & NVP are present in decreasing concentration for 7 days after stopping

When stopping, give at least 7 days of fully active ART regimen to prevent EFV or NVP resistance from developing during the “tail”
ART Adverse Effects, medication interactions

These are numerous, and difficult to remember
- The Liberian treatment guideline has an excellent symptom-based guide to adverse effects and complications

For medication interactions – focus on a few high-yield culprits and forget the rest, just use:

https://hiv-druginteractions.org/
Nucleoside Reverse Transcriptase Inhibitor (NRTI) – Adverse Effects & Caution

**tenofovir [TDF]**
- Fully active against HBV
- Dose adjust if CrCl <50 (q48hr for CrI 30-49, q72 for 10-29)
- Renal Toxicity / Fanconi Syndrome
  - Glucosuria, proteinuria, aciduria, CKD, hyperphos, hypoK
- Osteoporosis
- Tenofovir alafenamide (TAF)

**lamivudine [3TC]**
- Well tolerated
- In all 1st & 2nd line regimens
- HBV-active but not preferred for mono-therapy
- Decrease dose for CrCl <50

**abacavir [ABC]**
- Hypersensitivity reaction = absolute contraindication
- Increases cardiovascular disease risk
- No renal dose adjustment in CKD

**zidovudine [AZT]**
- Q 12 hour dosing
- Bone marrow suppression = anemia & leukopenia
- myopathy
- lipodystrophy
- Lactic acidosis (rare if not co-administered with stavudine)
- Dose adjust for CrCl <15 – take 300mg daily
Nucleoside Reverse Transcriptase Inhibitor (NRTI) – Adverse Effects & Caution (cont)

stavudine [d4t]

- Not included in Liberia 5th edition guideline
- Peripheral neuropathy
- Lactic acidosis (esp in combination with AZT)
- lipodystrophy
- dyslipidemia
Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) – Adverse Effects & Caution

<table>
<thead>
<tr>
<th>Nevirapine [NVP]</th>
<th>Efavirenz [EFV]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypersensitivity reaction</strong></td>
<td></td>
</tr>
<tr>
<td>• Rash and/or hepatotoxicity, may be with fever, renal injury, mucous membrane involvement</td>
<td></td>
</tr>
<tr>
<td>• Most common in women, those with HBV co-infection &amp; high CD4</td>
<td></td>
</tr>
<tr>
<td>• Caution if CD4 is:</td>
<td></td>
</tr>
<tr>
<td>• &gt;250 in women</td>
<td></td>
</tr>
<tr>
<td>• &gt;400 in men</td>
<td></td>
</tr>
<tr>
<td><strong>Neuropsychiatric effects</strong></td>
<td></td>
</tr>
<tr>
<td>• Nightmares, depression, psychosis, ↑ suicidality, headache</td>
<td></td>
</tr>
<tr>
<td>• Take at bedtime on empty stomach to minimize adverse effects</td>
<td></td>
</tr>
<tr>
<td>• ~15% erythematous maculopapular exanthema</td>
<td></td>
</tr>
<tr>
<td>• Hepatotoxicity – do not use if cirrhosis CTP Class B or C</td>
<td></td>
</tr>
<tr>
<td>• Unfavorable lipid profile effects</td>
<td></td>
</tr>
<tr>
<td>• Gynecomastia</td>
<td></td>
</tr>
<tr>
<td>• QTc prolongation</td>
<td></td>
</tr>
</tbody>
</table>

No renal dose adjustment!
Protease Inhibitor (PI) – Adverse Effects & Caution

**lopinavir / ritonavir [LPV/r]**
- Diarrhea
- Hyperlipidemia
- Liquid formulation is 40% alcohol by volume

**atazanavir / ritonavir [ATV/r]**
- Benign hyperbilirubinemia
- Nephrolithiasis

**darunavir + ritonavir [DRV+r]**
- Abdominal pain, diarrhea
- Rash (within 4wks of start, self-resolves)

**ritonavir [r]**
- Inhibits liver enzyme CYP3A
- MANY drug-drug-interactions
- Diarrhea, nausea, abdominal pain

No renal dose adjustment!
Integrase Strand Transfer Inhibitor (INSTI) - Adverse Effects & Caution

**Dolutegravir [DTG]**

- Mild side effects: headache, insomnia, nausea – generally self-resolve
- If known liver disease (ie, HBV) -> check LFTs before & after initiation
- BID with rifapentine for MTB treatment
- Neural tube defects if taken at conception
  - Tsepamo Study: NTD in 3/1,000 on DTG vs 1/1,000 on other ART
    - WHO now recommends DTG for use in women of childbearing age. Countries give varying recommendations.
- Increase in serum Creatinine (by ~0.15 on average) without CKD

No renal dose adjustment!
NNRTI & INSTI Key Drug-Drug Interactions

**nevirapine [NVP]**
- DO NOT give with: rifampicin or rifapentine

**efavirenz [EFV]**
- DO NOT give with: simvastatin
- AVOID with: clopidogrel
- May decrease level of: atorvastatin

**dolutegravir [DTG]**
- metformin should not exceed 1 gram total daily dose
- Separate from divalent cations (ie, iron, calcium, magnesium) – take DTG 2hrs before OR 6hrs after
Boosted PI Key Drug-Drug Interactions

**class-wide OR ritonavir**
- **Statins**: 20mg atorvastatin max; NO simvastatin
- Variable effects on **warfarin**
- Most **anti-convulsants** lower PI, NNRTI, INSTI levels
- Do NOT give with: **rifampicin, rifapentine**
- Increases concentration of: **Beta-blockers** (except atenolol, labetalol) & **calcium channel blockers**

**atazanavir / ritonavir [ATV/r]**
- **Antacids**: take ATV 2hrs before OR 1hr after antacid
- **H2 antagonist**: take with ATV/r OR 10hrs before ATV/r
- **PPI**: do not co-administer

**darunavir + ritonavir [DRV+r]**
- **PPI**: max 40mg omeprazole

**lopinavir / ritonavir [LPV/r]**
- No significant unique interactions
NRTI & NNRTI Switches by adverse effects

**Hypersensitivity Reaction:** fever, pain, emesis, cough

- **ABC** → **AZT**
- **AZT** → **TDF or ABC**
- **TDF** → **ABC or AZT**

**Anemia, lipodystrophy, lactic acidosis**

- **AZT** → **TDF or ABC**
- **ABC** → **AZT**

**Renal failure**

**Any suspected hypersensitivity reaction = STOP the ART & DO NOT re-challenge**

**Hypersensitivity Reaction:** fever, rash, hepatitis

- **NVP** → **EFV**
- **EFV** → **NVP**

**Neuropsychiatric, gynecomastia, hepatitis/rash**

- **NVP** → **EFV**
- **EFV** → **NVP**

**Give dizziness, drowsiness & nightmares 4 weeks to resolve**
PI & INSTI Switches by adverse effects

- **ATV/r**
  - Jaundice (benign if only indirect bilirubin is elevated)
  - Diarrhea, vomiting, headache, dizziness

- **LPV/r**
  -

- **EFV**
  - Headache, insomnia, diarrhea, hepatitis

- **DTG**
  -
## Start by clinical scenario

<table>
<thead>
<tr>
<th>Condition</th>
<th>Timing of ART start</th>
<th>ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia (&lt;8g/dl)</td>
<td>NOW</td>
<td>DTG / TDF / 3TC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pedi: DTG + ABC / 3TC</td>
</tr>
<tr>
<td>Active MTB</td>
<td>Within 14 days</td>
<td>DTG / TDF / 3TC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pedi &lt;30kg: EFV</td>
</tr>
<tr>
<td>Jaundice</td>
<td>Initial evaluation first</td>
<td>EFV / TDF / 3TC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DTG only if severe liver dz &amp; HBV/HCV ruled out</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>Within 7 days</td>
<td>NVP + ABC/3TC</td>
</tr>
<tr>
<td>Psychiatric Illness History</td>
<td>NOW</td>
<td>DTG / 3TC / TDF</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NVP + TDF / 3TC</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>NOW</td>
<td>DTG / TDF / 3TC</td>
</tr>
<tr>
<td>New HIV+ in labor</td>
<td>NOW</td>
<td>DTG / TDF / 3TC</td>
</tr>
</tbody>
</table>
Cases

55yoM with CKD recently started on DTG/ABC/3TC develops a cough and vomiting 2 weeks after starting.
  ◦ What is going on? Do you switch ART, and if so to what?

23yoF planning pregnancy soon sees you in clinic for new HIV diagnosis & ART start.
  ◦ How do you counsel her on ART options?

34yoF presents with suicidal ideation after starting ART recently. She does not know her meds and medical records are missing.
  ◦ What ART might she be on, and what do you suggest?
Cases

59yoM with HTN on NVP/TDF/3TC presents with 20lb weight loss and polyuria over 3 months.
  ◦ What do you suspect? What studies do you order? What is your recommendation?

63yoF on NVP/AZT/3TC notes an increasingly protuberant abdomen and thinning facial soft tissue.
  ◦ What do you suspect? What is your recommendation?

33yoM on NVP/TDF/3TC has VL 2,350 after IAC and 3 months of good adherence.
  ◦ What is your recommendation?

43yoF on LPV/r/TDF/3TC with chronic diarrhea without weight loss for 3 months.
  ◦ What do you suspect? What is your recommendation?
References


