Focused Review of Antiretroviral Treatment

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Session 1 & 2 Review
ART Regimen: Building Blocks

3 meds
- 2 fully active
- PI needs a ritonavir “booster”

**Inhibits** CYP 450-3A4

concentration of PI

### Core

- INSTI
- PI
- NNRTI

### Backbone

- NRTI + NRTI
- NRTI + NRTI
- NRTI + NRTI
Nucleoside Reverse Transcriptase Inhibitor (NRTI)

Tenofovir [TDF]
- Need for HIV-HBV co-infection [alternative = entecavir]
- Dose reduction for CrCl <50

Lamivudine [3TC]
- Well tolerated
- In all 1st & 2nd line regimens

Abacavir [ABC]
- Hypersensitivity reaction = absolute contraindication

Zidovudine [AZT]
- Q12hr dosing
- NOT if hgb <8
- Watch for anemia

Available Combo Pills
- ABC/3TC
- TDF/3TC
- AZT/3TC

Diagram:
- DNA → Reverse transcription → RNA
- DNA polymerisation blocked
- NRTIs

Core + Backbone

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SIB Swiss Institute of Bioinformatics
Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI)

**Nevirapine (NVP)**
- 1st line, but not for ART start
- SE: hypersensitivity reaction, rash, hepatitis

**Efavirenz (EFV)**
- 1st line, but not for ART start
- SE: neuropsych, insomnia, nightmares, dizziness, gynecomastia

Available Single Tablet Regimen
- AZT / 3TC / NVP
- TDF / 3TC / EFV – “B+”
  - Very similar to “Atripla”
Protease Inhibitor (PI)

Lopinavir / ritonavir [LPV/r – Kaletra]
- 2nd line
- diarrhea

Atazanavir / ritonavir [ATV/r]
- 2nd line
- Do NOT use with rifampicin for MTB tx
- Benign hyperbili/jaundice

Darunavir / ritonavir [DRV + r]
- 3rd line
- Must take separately

Not Available in Single Tablet Regimen

Core + Backbone

NRTI + NRTI

+ booster

PI

Backbone

Core

Not Available in Single Tablet Regimen
Integrase Strand Transfer Inhibitor
INSTI

Dolutegravir [DTG]
- **1st line** for patients 30kg + without childbearing potential
- WHO: 1st line treatment for pregnant women
- SE mild: HA, insomnia, nausea
  - Check LFTs before/after initiation if known liver disease
  - BID with rifapentine for MTB treatment

**Available Single Tablet Regimen**
- TDF / 3TC / DTG

**Core**
- INSTI

**Backbone**
- NRTI + NRTI
ART key

- **DTG** (dolutegravir)
- **ATV/r** (atazanavir / ritonavir)
- **LPV/r** (lopinavir / ritonavir)
- **DRV + r** (darunavir / ritonavir)
- **NVP** (nevirapine)
- **EFV** (efavirenz)
- **TDF** (tenofovir)
- **ABC** (abacavir)
- **3TC** (lamivudine)
- **AZT** (zidovudine)
First Line ART

START

Core

Men 30kg
Women 45yo +

Women of "B+
childbearing potential

Patients < 30kg

Backbone

DTG / TDF / 3TC

EFV / TDF / 3TC

NVP / AZT / 3TC

Not for START

Core

Backbone

DTG +

AZT / 3TC

ABC / 3TC

EFV +

AZT / 3TC

NVP +

TDF / 3TC

ABC / 3TC
2nd line ART

Not for START*

Core + Backbone:
- ATV/r + [TDF / 3TC, AZT / 3TC]
- LPV/r + [TDF / 3TC, ABC / 3TC, AZT / 3TC]

*1st line START for < 3yo IF extra support
3\textsuperscript{rd} line ART

2 Core Agents

\begin{align*}
\text{DRV + r} & + \text{DTG}^* \\
\text{*DTG is BID if INSTI resistance}
\end{align*}

Backbone

\begin{align*}
\text{TDF} & / \text{3TC} \\
\text{ABC} & / \text{3TC} \\
\text{AZT} & / \text{3TC}
\end{align*}

Assumes likely resistance to at least 2 prior agents

- Assumes failure to prior treatment with core of:
  \begin{align*}
  \text{ATV/r} & \quad \text{or} \quad \text{LPV/r} \quad \text{or} \quad \text{DTG}
  \end{align*}

- For likely NRTI resistance, “flip” the backbone (or follow genotype)
  \begin{align*}
  \text{If failed on:} & \quad \text{Switch to:} \\
  \text{ABC} & \quad \text{or} \quad \text{TDF} \quad \rightarrow \quad \text{AZT} \\
  \text{AZT} & \quad \rightarrow \quad \text{TDF}
  \end{align*}
Initial Treatment Failure (go to Alt 1)

**NNRTI-based**
- Confirmed virologic failure
  - ATV/r
  - AZT / 3TC or TDF / 3TC if prior TDF/3TC

**ATV/r-based** or **LPV/r-based**
- Confirmed virologic failure
  - DRV + r
  - DTG
  - AZT / 3TC or TDF / 3TC if prior TDF/3TC

**DTG-based**
- Confirmed virologic failure
  - ATV/r
  - AZT / 3TC or TDF / 3TC if prior TDF/3TC
NRTI & NNRTI Switches by adverse effects

Hypersensitivity Reaction: fever, pain, emesis, cough
- ABC → AZT

Anemia, lipodystrophy, lactic acidosis
- AZT → TDF or ABC

Renal failure
- TDF → ABC or AZT

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

Hypersensitivity Reaction: fever, rash, hepatitis
- NVP → EFV

Neuropsychiatric, gynecomastia, hepatitis/rash
- 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**
  - Headache, insomnia, diarrhea, hepatitis

- **DTG**
  - Headache, insomnia, diarrhea, hepatitis
Case

32 year old female

- Weight loss and diarrhea for 6 months
- BMI now 18
- HIV diagnosed by rapid testing 1 month ago

How do you counsel?

What is your next step?
Case (cont)

1 months later you see her in clinic
  ◦ Reports full adherence
  ◦ Diarrhea has stopped, weight is same as on start
  ◦ Notes that she has been feeling depressed

What do you review?

What are your next steps?
Case (cont)

She returns for 2\textsuperscript{nd} month review

\begin{itemize}
  \item Nightmares developed
  \item She has stopped her ART for the past 2 weeks entirely
\end{itemize}

What is your next step?
Case (cont)

You have switched your patient to a DTG-based regimen. Her 6 month viral load returns 
**detectable** but < 1,000.

What is your next step?
Case (cont)

She discloses that her husband is a truck driver who travels a 3-day route each week. She has not disclosed to him for fear of his reaction and therefore does not take ART on days when he is home to avoid inadvertent disclosure.

How do you respond?
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?