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2020-04-17

Focused Review of Antiretroviral Treatment

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Repository Citation
Younkin M. (2020). Focused Review of Antiretroviral Treatment. PEER Liberia Project. https://doi.org/10.13028/q57k-mm25. Retrieved from https://escholarship.umassmed.edu/liberia_peer/72

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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		Backbone		
INSTI	+	NRTI	+	NRTI
PI	+	NRTI	+	NRTI
NNRTI	+	NRTI	+	NRTI

Nucleoside Reverse Transcriptase Inhibitor NRTI

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

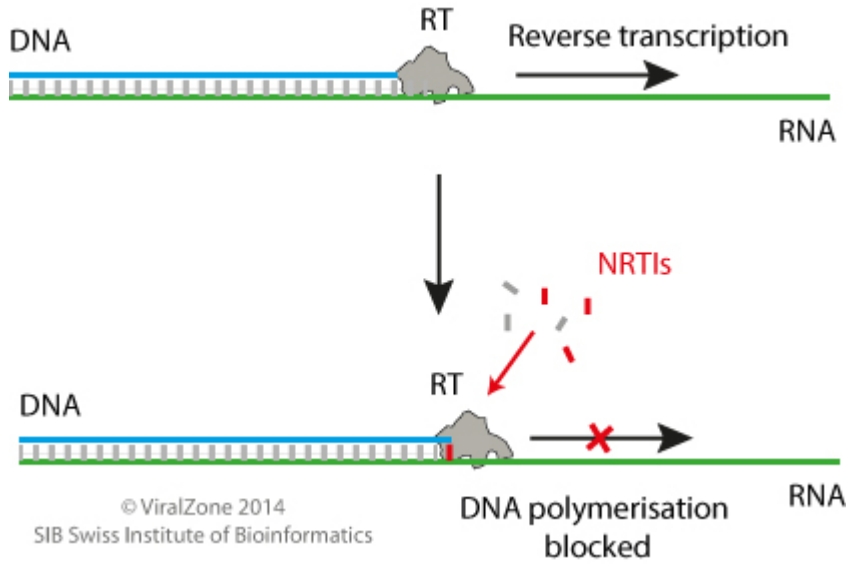
Lamivudine [3TC]
- Well, tolerated
- in all 1st & 2nd line regimens

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

Core		Backbone		
?	+	NRTI	+	NRTI



Non-Nucleoside Reverse Transcriptase Inhibitor NNRTI

Nevirapine [NVP]

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

Efavirenz [EFV]

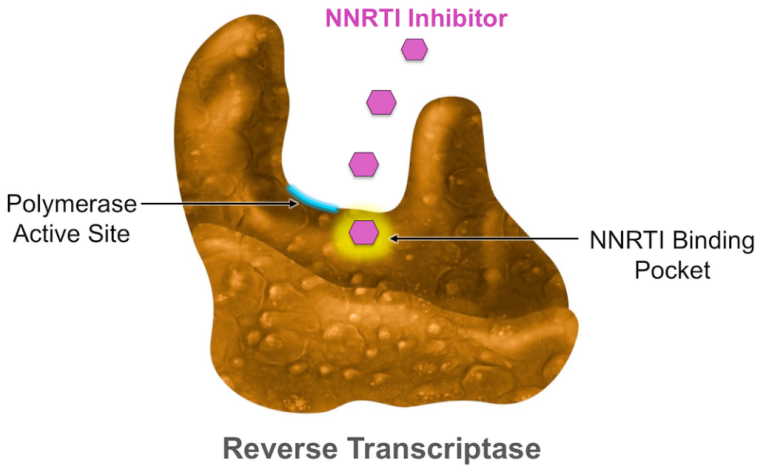
- **1st line**, but not for ART start
- SE: neuropsych, insomnia, nightmares, dizziness, gynecomastia

Available Single Tablet Regimen

- AZT / 3TC / NVP
- TDF / 3TC / EFV – "**B+**"
  - Very similar to "Atripla"

Core Backbone

NNRTI + NRTI + NRTI



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

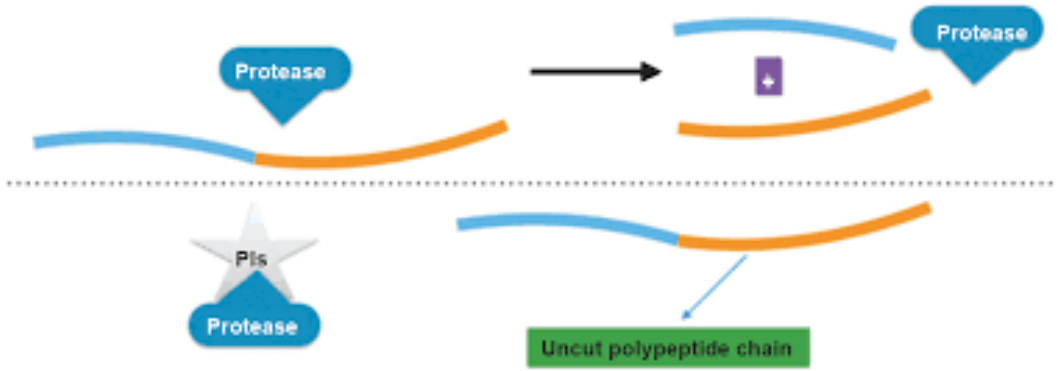
Darunavir / ritonavir [DRV + r]
- 3rd line
- Must take separately

Not Available in Single Tablet Regimen

Core + Backbone

PI + NRTI + NRTI

booster



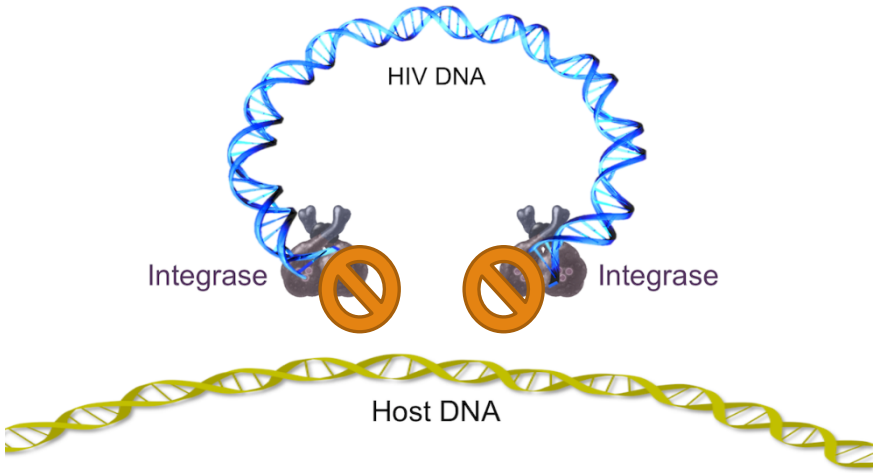
Integrase Strand Transfer Inhibitor INSTI

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

Core | Backbone

INSTI + NRTI + NRTI



Available Single Tablet Regimen

- TDF / 3TC / DTG

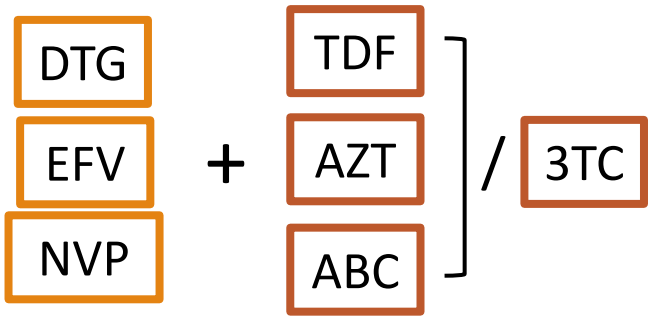
ART key

DTG	dolutegravir
ATV/r	atazanvir / ritonavir
LPV/r	lopinavir / ritonavir
DRV + r	darunavir / ritonavir

NVP	nevirapine
EFV	efavirenz

TDF	tenofovir	ABC	abacavir
3TC	lamivudine	AZT	zidovudine

First Line ART



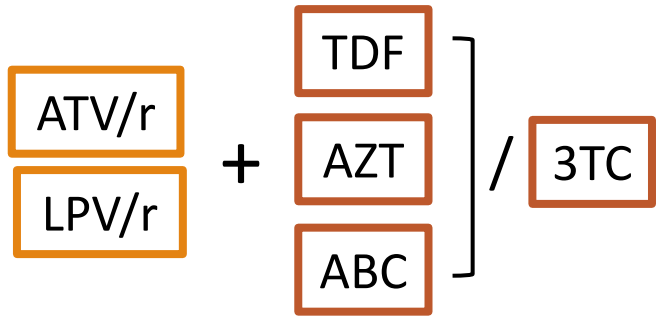
START

	Core		Backbone		
Men 30kg Women 45yo +	DTG	/	TDF	/	3TC
Women of childbearing potential	EFV	/	TDF	/	3TC
Patients < 30kg	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]

Core Backbone

LPV/r + [TDF / 3TC; ABC / 3TC; AZT / 3TC]

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

3rd line ART

2 Core Agents

DRV + r + DTG*

*DTG is BID if INSTI resistance

Backbone

- TDF / 3TC
- ABC / 3TC
- AZT / 3TC

Assumes likely resistance to at least 2 prior agents

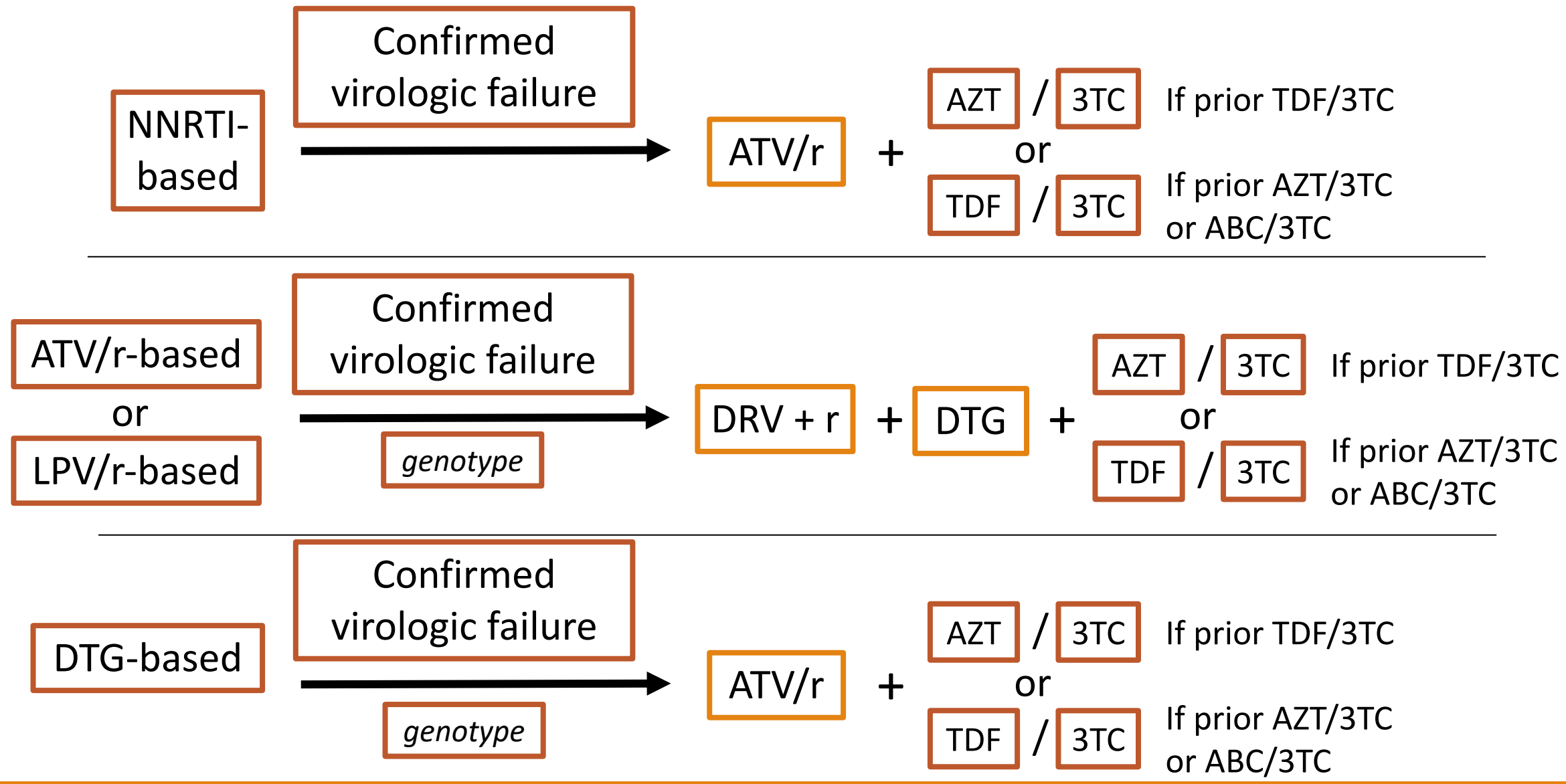
- Assumes failure to prior treatment with core of:

ATV/r or LPV/r or DTG

- For likely NRTI resistance, "flip" the backbone (or follow genotype)

If failed on:		Switch to:
ABC or TDF	→	AZT
AZT	→	TDF

Initial Treatment Failure (go to Alt 1)



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

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

Hypersensitivity Reaction: fever, rash, hepatitis

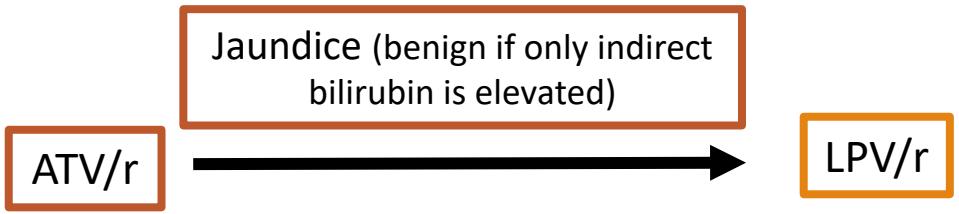
NVP → EFV

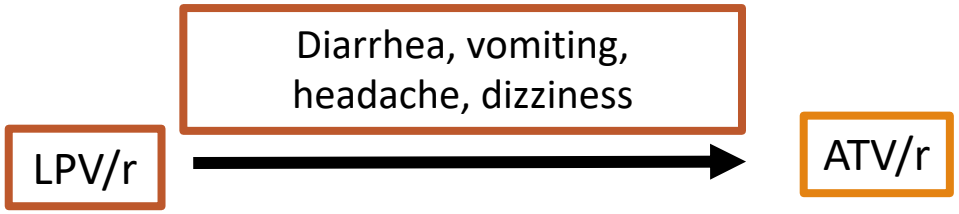
Neuropsychiatric, gynecomastia, hepatitis/rash

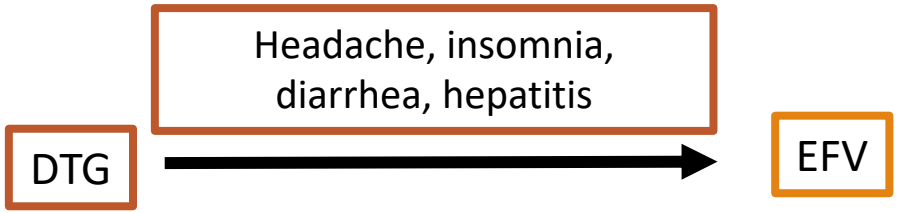
EFV → NVP

Give dizziness, drowsiness & nightmares 4 weeks to resolve

PI & INSTI Switches by adverse effects







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 2nd month review

- Nightmares developed
- She has stopped her ART for the past 2 weeks entirely

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?