When and How To Switch

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1

Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years:

Dr Lehmann has no relevant financial relationships with ineligible companies to disclose. (Updated 12/14/22)

Slide 2

2

Learning Objectives

After attending this presentation, learners will be able to:

- Switch antiretroviral therapy (ART) in the setting of viral suppression
- Switch ART to long-acting cabotegravir and rilpivirine
- Switch ART for virologic failure

Slide 3

3

Should I simplify an initial regimen?

Slide 4

4

Case 1
Man, 53 Years

May 2015:

- Diagnosed HIV infection
- HIV encephalopathy (multiple cerebral seizures at initial diagnosis)
- Nicotine abuse
- Arterial hypertension
- Hypercholesterolemia

- CD4 nadir 200/µl (12%), HIV: 850,000 cop/ml.

ART History:

- Start: DTG/3TC/ABC

Good tolerability
Very good HIV surrogate parameters

- HIV-RNA < 20 cop/ml
- CD4 250/µl (16%)

Summer 2021

- STEMI of the posterior wall with acute coronary syndrome.
- Recanalization, stent implantation

Slide 5

5

ARS Question 1: What would you do?

A. Continue his current ART
B. Change his ABC/3TC to TAF / FTC containing regimen
C. Change to DTG/3TC
D. Some other option

Slide 6

6

Can I switch patients with viral suppression in the setting of M184V or K65R mutations

Slide 7

7

Case 2

Woman, 42 years

Winter 2019:

- Diagnosed HIV infection
- cerebral Toxoplasmosis
- Late Presenter

Initial:
- CD4 nadir 150/µl (15%)
- HIV: 650,000 cop/ml

Resistance- Testing:

NRTI: M184V
NNRTI: none
PI: none
InSTI: none

Start ART 2019:

TAF/ FTC/ DRV/r

Surrogate Parameters:

- HIV-RNA < 20 cop/ml
- CD4 400/µl (35%)

Slide 8

8

ARS Question 2: What would you propose?

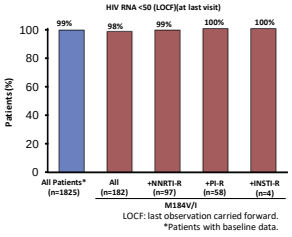
A. TDF / 3TC/DOR
B. FTC/TAF/BIC
C. FTC/TAF/DRV/c
D. TAF/FTC/DTG
E. Other option

Slide 9

9

High Efficacy of Switching to Bictegravir/FTC/TAF with Suppressed HIV and pre-existing M184V/I

- Pooled data from 6 trials in which PWH and virologic suppression switched to B/F/TAF (n=1825 with baseline data)
- Preexisting M184V/I identified in 182 participants (10%)
- 98% of participants with pre-existing M184V/I maintained viral suppression



LOCF: last observation carried forward.
*Patients with baseline data.

Slide 10

10

Should I switch to Long-acting Cabotegravir and Rilpivirine?

Slide 11

11

CASE 3
AR, WOMEN 59 YEARS, KENYA

May 2002:

- Diagnosed HIV infection
- Cured hepatitis B
- Arterial hypertension
- Hypercholesterolemia

ART History:

- 03/05-08/05: AZT/3TC +CCR5 (Study)
- 08/05-03/10: ART break
- 03/10-05/15: EFV/TDF/FTC
  05/15-09/16: TDF/FTC/RPV
- Since 09/16: FTC/TAF/RPV

Good tolerability
Very good HIV surrogate parameters (09/21)

- HIV-RNA < 20 cop/ml
- CD4 400/µl (35%)

Concomitant-Medication:

- Candesartan 8 mg 1-0-0
- Atorvastatin 20mg 1-0-0

Spring-Summer 2021:

- Complaints about taking medication every day

Slide 12

12

ARS Question 3: At this point what would you propose?

A. Talk to her and keep her on her current Rx (FTC/TAF/RPV)
B. Resistance analysis on proviral HIV level
C. CAB / RPV i.m.
D. Some other option

Slide 13

13

LONG ACTING CABOTEGRAVIR (CAB) AND RILPIVIRINE (RPV)

Indication

Approved for treatment only in combination in patients

- Who are currently virologically suppressed on a stable antiretroviral regimen (HIV-1 RNA < 50 copies/mL)
- Without current or historically documented resistance to the NNRTI or INI class of drugs
- Without a history of virologic failure to NNRTI- and INI-class agents.

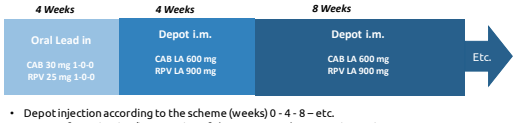
Contraindications

- Active HBV infection unless also receiving an oral HBV active regimen
- Pregnancy or plans to become pregnant
- Receiving medications with significant drug interactions with CAB or RPV

Slide 14

14

DOSING

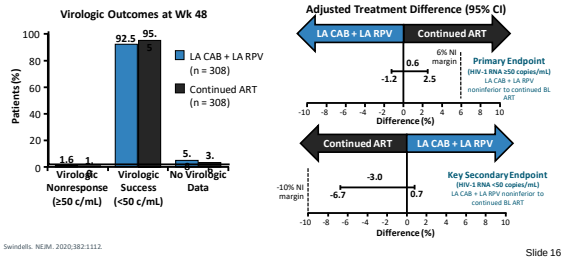


- Depot injection according to the scheme (weeks) 0 - 4 - 8 – etc.
- In case of termination/interruption of therapy, an oral suppressive regimen must be taken 4 weeks after the first injection or 8 weeks after the second/later injection.

Slide 15

15

EFFICACY- ATLAS: Switch to LA CAB + RPV vs Continued 3-Drug ART in Virologically Suppressed Adults



Swindells. NEJM. 2020;382:1112.

Slide 16

16

How do I manage virologic failure ?

Slide 17

17

Case 4
Man 46 Years, Nigeria

May 2018:

- Diagnosed HIV infection
- Initial:
- CD4 nadir 250/µl (15%), HIV: 450,000 cop/ml (wild type)

ART History:

- Start: TDF / FTC / EFV

Good tolerability
Very good HIV surrogate parameters

Spring 2019

- HIV-RNA < 40 cop/ml
- CD4 450/µl (21%)

Fall 2021

- HIV-RNA 12.000 cop/ml
- CD4 /µl 270 (16%)

Resistance- Testing:

NRTI: M184V

NNRTI Resistenz
PI
InSTI

Slide 18

18

ARS Question 4: At this point which regimen would you choose?

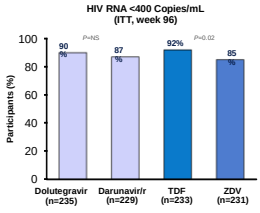
A. TDF / 3TC / DTG
B. ABC/ 3TC / DTG
C. TDF / 3TC / DRV/r
D. FTC/TAF/BIC
E. Some other option

Slide 19

19

NADIA: 2nd-Line ART after NNRTI Failure

- Participants with virologic failure on TDF/3TC/NNRTI (n=464)
- Randomized to switch to DTG or DRV/r with either TDF/3TC or AZT/3TC
- Study participants:
  - CD4 ≤200: 51%; VL ≥100,000: 28%
  - Resistance: K65R/N: 50%; M184V: 86%
- DTG + 2 NRTIs non-inferior to DRV/r + 2 NRTIs
  - High rate of suppression even when no NRTIs predicted to be active!
- Continuing TDF/3TC superior to switch to AZT/3TC
- 9 participants (4%) in DTG group developed resistance; no resistance in the DRV/r group



Paton N, Lancet, 2022

Slide 20

20

Conclusions

- Persons with suppressed virus and no history of transmitted or acquired HIV drug resistance can generally switch therapy to any of the recommended initial regimens (BIC/TAF/FTC, DTG plus TXF/XTC or DTG/3TC) and maintain viral suppression.
- In persons with viral suppression switching to DTG plus 2 nRTIs or BIC/FTC/TAF, even in the setting of likely or proven nRTI resistance (M184V and K65R mutations) is safe.
- 2-drug regimens (DTG/3TC or DTG/RPV): unless there is documented or suspected history of treatment failure, proviral resistance testing is not required prior to switching to 2-drug therapy, even if there is no available pretreatment resistance test result (evidence rating: BII)
- Long-acting CAB + RPV is safe and effective ART for PLWH with proven viral suppression for at least 3 months and no history of treatment failure and no known or suspected resistance to CAB or RPV

Slide 21

21

22