Interactive ART Cases From the Clinic(ians): Case-Based Panel Discussion

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Learning Objectives

After attending this presentation, learners will be able to select antiretroviral therapy in patients who:

- Are starting initial therapy
- Have persistently low-level viremia
- Have a baseline M184V mutation
- Are pregnant
- Are eligible for PrEP

Question

Seems like we are now starting ARV therapy for about everyone, what about starting therapy immediately at time of diagnosis?

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Case 1

- 30 yo Female was diagnosed with HIV infection 4 hours ago in the ER
- Asymptomatic
- **Initial:** HIV RNA 17,000 c/ml (HIV DNA positive)
  CD4 count 470 cells/ul
- Other labs are normal; HLA-B57 neg
- Genotype determined from DNA is wild-type
- No prior medical history.
- Ok to start therapy if you think she should

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ARS Question 1: When would you choose to start therapy?

1. Right now in the ER
2. Within 1 - 2 days (outpt Clinic)
3. In the next 2 weeks (outpt Clinic)
4. Within 2 – 4 weeks
5. Some other option

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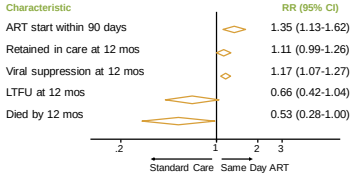
Improved Clinical Outcomes With Rapid ART Initiation

- Universal recommendations for treating all HIV-infected persons
- Systematic review of 22 studies of rapid ART initiation (including 4 RCTs)



Ford N, et al. AIDS. 2018;32:17-23.

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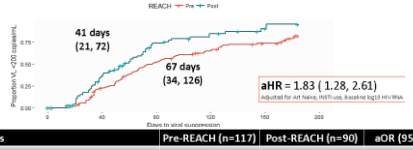
Expedited ART– Experience in Atlanta

- Grady reduced barriers, with goal to begin ART within 72hrs
- Pre-intervention days to ART = 22, Post-intervention days to ART= 4.



Outcomes	Pre-REACH (n=117)	Post-REACH (n=90)	aOR (95% CI)
Attended 1st scheduled appointment[†]	85 (73)	73 (81)	1.63 (0.82, 3.22)
Achieved viral suppression[¥]	87 (74)	61 (68)	0.77 (0.39, 1.52)

[†]Adjusted for age, race, sex and being ART Naïve
[¥]Adjusted for age, race, baseline HIV RNA & INSTI use

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Question

What regimen should I use as initial therapy?

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Case 2

- 48 yo Male presents with newly diagnosed HIV infection
- Asymptomatic
- **Initial:** HIV RNA 28,000 c/ml
  CD4 count 650 cells/ul
- Other labs are normal; HLA-B57 positive
- Genotype is Wild-type virus
- No prior medical history. Normal renal function
- Ok to start therapy if you think he should

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ARS Question 2: At this point which regimen would you choose?

1. TDF / 3TC / low dose (400mg) EFV (fdc; generic)
2. ABC/ 3TC / DTG (fdc)
3. TAF/ FTC (fdc) + DTG
4. TAF / FTC/ ELV / cobi (fdc)
5. TAF/ FTC / BIC (fdc)
6. TAF / FTC (fdc) + RAL (once daily)
7. TAF / FTC / RPV (fdc)
8. TAF/ FTC (fdc) + DRV/r (or cobi / fdc)
9. Some other option (e.g., DRV/r + DTG or …)

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JAMA | Special Communication

Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults
2018 Recommendations of the International Antiviral Society-USA Panel

Michael S. Saag, MD; Constance A. Benson, MD; Rajesh T. Gandhi, MD; Jennifer F. Hoy, MBBS; Raphael J. Landovitz, MD; Michael J. Mugavero, MD, MHSc; Paul E. Sax, MD; Davey M. Smith, MD; Melanie A. Thompson, MD; Susan P. Buchbinder, MD; Carlos del Rio, MD; Joseph J. Eron Jr, MD; Gerd Fätkenheuer, MD; Huldrych F. Günthard, MD; Jean-Michel Molina, MD; Donna M. Jacobsen, BS; Paul A. Volberding, MD

IMPORTANCE Antiretroviral therapy (ART) is the cornerstone of prevention and management of HIV infection.

Editorial page 1
Author Audio Interview
Related article page 1

Saag MS, Benson CA, Gandhi RT, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2018 recommendations of the International Antiviral Society-USA Panel. *JAMA*. 2018;320(4):1-18.

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Recommended Initial Regimens: InSTI Plus 2 nRTIs

- Bictegravir/TAF/emtricitabine
- Dolutegravir/abacavir/lamivudine
- Dolutegravir plus TAF/emtricitabine

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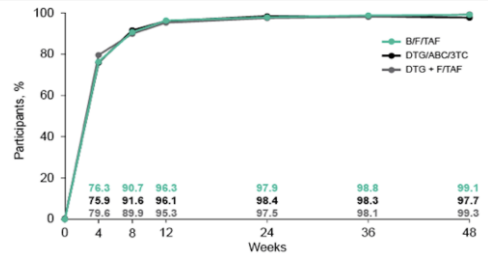
Saag, Benson, Gandhi, et al, JAMA, 2018

Virologic Response by Visit (FAS)

HIV-1 RNA <50 copies/mL, Missing=Excluded Analysis



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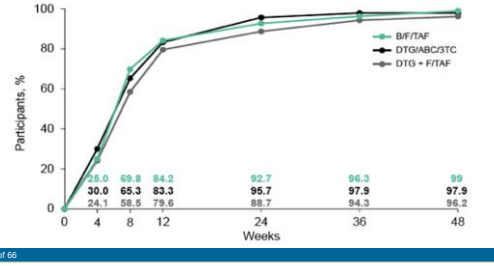
22nd IAS, 23-26 July 2018, Amsterdam, Netherlands

Virologic Efficacy:
HIV-1 RNA <50 copies/mL, Missing=Excluded Analysis

Baseline HIV-1 RNA >100,000 copies/mL



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Recommended Initial Regimens: If an InSTI Is Not Available

- Darunavir/cobicistat/TAF (or TDF)/emtricitabine*
- Darunavir boosted with ritonavir plus TAF (or TDF)/emtricitabine
- Efavirenz/TDF/emtricitabine
- Elvitegravir/cobicistat/TAF (or TDF)/emtricitabine
- Raltegravir plus TAF (or TDF)/emtricitabine
- Rilpivirine/TAF (or TDF)/emtricitabine (if pretreatment HIV RNA level is <100,000 c/mL and CD4 cell count is >200/µL)
- Fixed-dose Dor/TDF/3TC tablet approved July 2018

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Saag, Benson, Gandhi, et al, *JAMA*, 2018.

ARS Question 3: Would you use DTG / 3TC as initial therapy?

1. Yes
2. No
3. Not sure

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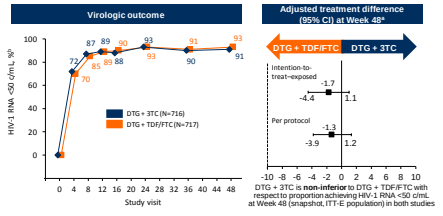
Gemini Studies: DTG plus 3TC vs. DTG plus TDF/FTC in Treatment Naïve patients.



[a]Based on Cochran-Mantel-Haenszel stratified analysis adjusting for the following baseline stratification factors: plasma HIV-1 RNA (≤100,000 vs >100,000 c/mL) and CD4+ cell count (≤200 vs >200 cells/mm^3). [b]Calculated from a repeated measures model adjusting for study treatment, visit (repeated factor), baseline plasma HIV-1 RNA, baseline CD4+ cell count, treatment and visit interaction, and baseline CD4+ cell count and visit interaction.

Cahn et al. *Lancet*. 2018 [Epub ahead of print].

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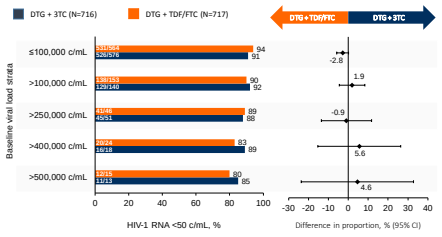
Eron et al. HIV DART and Emerging Viruses 2018; Miami, FL. Slides 7.

Proportion of Participants With Plasma HIV-1 RNA <50 c/mL at Week 48 (Snapshot Analysis) by Baseline Plasma HIV-1 RNA



Cahn et al. *Lancet*. 2018 [Epub ahead of print].

Eron et al. HIV DART and Emerging Viruses 2018; Miami, FL. Slides 7.

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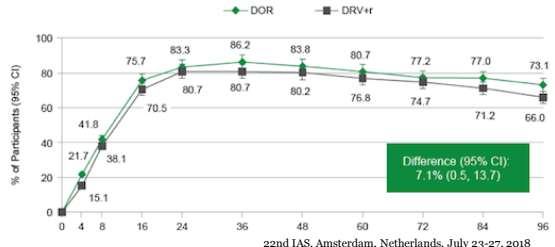
Figure 3. Proportion of Participants With HIV-1 RNA <50 c/mL†



22nd IAS, Amsterdam, Netherlands, July 23-27, 2018

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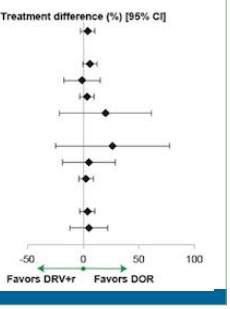
	HIV-1 RNA <50 c/mL, % (N) DOR	DRV/r
All Participants	81.0 (342)	76.8 (323)
Baseline HIV-1 RNA, c/mL		
≤100,000	85.6 (264)	79.7 (282)
>100,000	65.4 (78)	65.2 (72)
≤500,000	81.8 (325)	78.1 (311)
>500,000	64.7 (17)	36.4 (11)
Baseline CD4+ T-cell Count, cells/mm³		
≤50	80.0 (5)	52.9 (17)
>50 and ≤200	71.0 (31)	65.8 (38)
>200	82.0 (306)	79.9 (268)
NRTI Component		
TDF/FTC	80.3 (295)	76.3 (283)
ABC/3TC	85.1 (47)	80.0 (40)



22nd IAS, Amsterdam, Netherlands, July 23-27, 2018

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Question

Seems like we are now starting ARV therapy for about everyone, what about starting therapy for an **Elite Controller**?

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Case 3

- 30 yo Female was diagnosed with HIV infection 4 years ago
- Asymptomatic
- **Initial:** HIV RNA < 50 c/ml (HIV DNA positive)
  CD4 count 870 cells/ul
- Other labs are normal; HLA-B57 neg
- Genotype determined from DNA is wild-type
- No prior medical history.
- Ok to start therapy if you think she should

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ARS Question 4: Would you choose to start therapy at this time?

1. Yes
2. No
3. Maybe

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Question

Should I change a regimen when low level detectable virus is present?

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Case 4

- 55 yo male referred to you for evaluation
- Diagnosed 18 years ago with HIV infection
- **Initial:** HIV RNA 936,000c/ml
  CD4 count 70 cells/ul
- **Current:** HIV RNA 85 c/ml (prior value 62 c/ml)
  CD4 count 525 cells/ul
- Started on NEL/D4T/3TC; subsequently treated with
  - LOP-r / TDF/FTC,
  - EFV/ FTC/ TDF (fdc).
  - Now **DTG / DRV/c / 3TC**
- No historical resistance tests are available

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ARS Question 5: Should you change ARV therapy now?

1. Yes
2. No
3. Not sure

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Virologic Failure, Low Level Viremia, and Blips

Clinical characteristics

	≤6 months n=5,776	>6 to 12 months n=6,858	>12 months n=4,360
Pre-ART viral load *median*	**28000**	**62457**	**82713**
Year of ART initiation *median*	2011	2011	2011
ART anchor drug(s)			
NNRTI	40%	50%	46%
PI	32%	36%	45%
InSTI	**31%**	**16%**	**13%**
CD4 count, cells/μL *median*	440	460	460
AIDS diagnosis	**12%**	**14%**	**20%**
Hepatitis B co-infection	3%	4%	5%
Hepatitis C co-infection	**10%**	**9%**	**15%**

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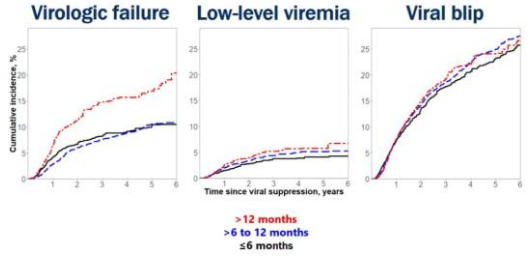
Lee, J et al NA-ACCORD, CROI 2019 Abst #97

Virologic Failure, Low Level Viremia, and Blips



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Lee, J et al NA-ACCORD, CROI 2019 Abst #97

Question

What regimen should I use as initial therapy in a women who desires to become pregnant?

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Case 5

- 30 yo Female who is on ARV Rx informs you she'd like to become pregnant HIV infection
- Asymptomatic; No prior medical history.
- **Initial:** HIV RNA 28,000 c/ml
  CD4 count 650 cells/ul
- Other labs are normal; HLA-B57 neg
- Pre-Rx genotype is Wild-type virus
- She is currently on DTG / ABC / 3TC (fdc) with undetectable HIV RNA

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ARS Question 6: At this point you would…

1. **Keep her on her current Rx** (ABC/ 3TC / DTG)
   Or Switch her to:
2. TDF / FTC / EFV (fdc)
3. TAF / FTC/ ELV / cobi (fdc)
4. TDF / FTC / RPV (fdc)
5. TDF/ FTC (fdc) / DRV/r
6. TAF/ FTC / ATV/r
7. TDF / FTC / ATV/r
8. Some other option

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ARS Question 7: Can she breastfeed if VL undetectable (U=U)?

1. Yes
2. No
3. I don't know

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Question

What regimen should be used as initial therapy when an M184V mutation is present?

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Case 6

- 30 yo Female presents with newly diagnosed HIV infection
- Asymptomatic
- **Initial:** HIV RNA 128,000 c/ml
  CD4 count 350 cells/ul
- Other labs are normal; HLA-B57 neg
- Genotype shows **M184V and K103N mutation**
- No prior medical history. No children. Does not plan to become pregnant.
- Ok to start therapy if you think she should

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ARS Question 8: At this point which regimen would you choose?

1. TDF / 3TC / low dose (400mg) EFV (fdc; generic)
2. DTG / 3TC (fdc)
3. ABC/ 3TC / DTG (fdc)
4. TAF/ FTC (fdc) + DTG
5. TAF / FTC/ ELV / cobi (fdc)
6. TAF/ FTC / BIC (fdc)
7. TAF / FTC (fdc) + RAL (once daily)
8. TAF / FTC / RPV (fdc)
9. TAF/ FTC (fdc) + DRV/r (or cobi / fdc)
10. Some other option (e.g., DRV/r + DTG or …)

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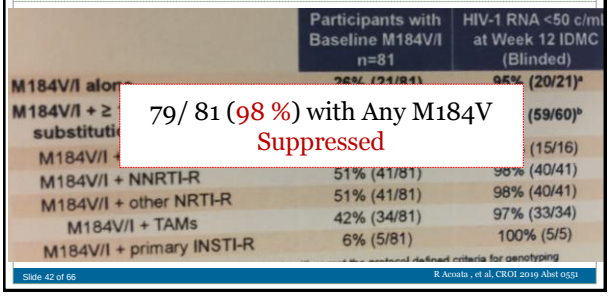
Pre-existing M184V Prior to Switch to InSTI Regimen: 4030



	Participants with Baseline M184V/I n=81	HIV-1 RNA <50 c/ml at Week 12 IDMC (Blinded)
M184V/I alone	26% (21/81)	95% (20/21)[a]
M184V/I + ≥ substituti		(59/60)[b]
M184V/I +		(15/16)
M184V/I + NNRTI-R	51% (41/81)	98% (40/41)
M184V/I + other NRTI-R	51% (41/81)	98% (40/41)
M184V/I + TAMs	42% (34/81)	97% (33/34)
M184V/I + primary INSTI-R	6% (5/81)	100% (5/5)

[a] This cohort defined criteria for genotyping

79/ 81 (98 %) with Any M184V Suppressed

R Acoata , et al, CROI 2019 Abst 0551

Question

Does InSTI therapy cause weight gain?

Case 7

- 47 year old woman starts on BIC/FTC/TAF 12 months ago from her original ARV regimen (TDF/FTC/DRV/r)
- Diagnosed 4 years ago
- **Initial:** HIV RNA 28,000 c/ml (Wildtype virus)
  CD4 count 450 cells/ul
- **Current:** HIV RNA <20 c/mL / CD4+ count 930 /uL
- Since starting her current regimen her weight has increased from **145 lbs to 171 lbs**

ARS Question 9: At this point you would…

1. **Keep her on her current Rx** (TAF/FTC/BIC)
   Or Switch her to:
2. TDF/ FTC (fdc) / DRV/r
3. TAF/ FTC / DRV/c (fdc)
4. TDF / FTC / RPV (fdc)
5. DTG / RLP (fdc)
6. TAF / FTC / ATV/c
7. Some other option

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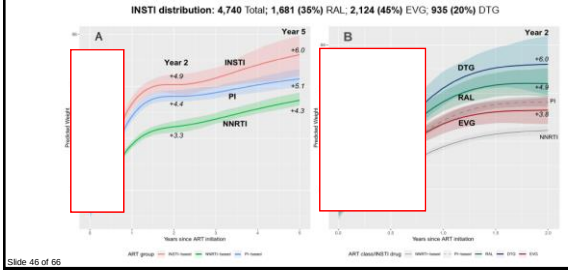
Change in Weight Overtime – NA-ACCORD

Bourgi et al CROI 2019



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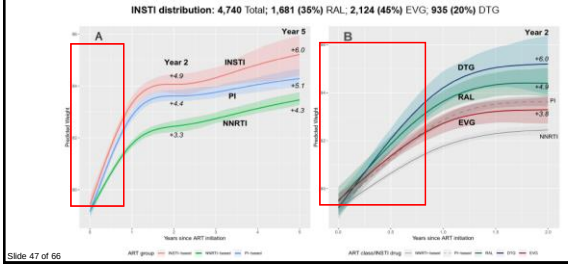
Change in Weight Overtime – NA-ACCORD

Bourgi et al CROI 2019



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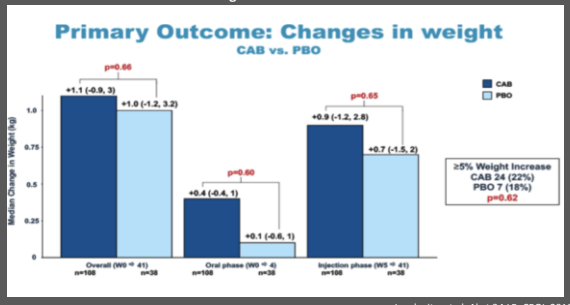
Cabotegravir vs Placebo for PrEP



Landovitz, et al, Abst 34 LB, CROI 2019

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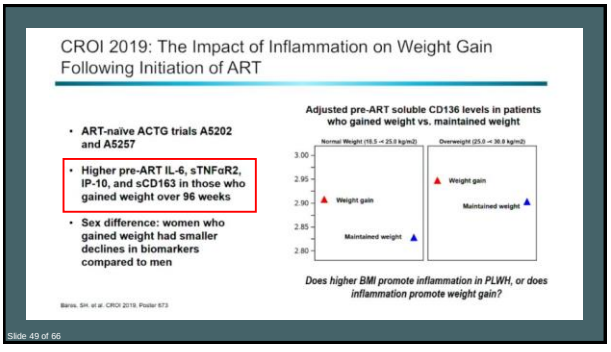

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Question

What should I use for PrEP Rx?

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Question

Should I simplify an "older" complex regimen?

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Case 9

- 57 year old man transfers to your care; no prior resistance tests are available
- He diagnosed with HIV in 2001; prior opportunistic infections and complains of 'Pill Fatigue'
- Has taken most existing antiretroviral drugs available; no exposure to DTG, ELV, or BIC
- Currently on TDF / FTC / ETV / DRV-r /Ral (twice daily)
- CD4+ count 430 /uL (nadir CD4 = 6)
  - HIV RNA <20 c/mL (max VL 667,000)

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ARS Question 11: At this point which regimen would you choose?

1. Continue current therapy (7 pills)

OR switch to:

2. TAF / FTC/ ELV / c (fdc) /DRV (2 pills)
3. ABC/ 3TC / DTG (fdc) / DRV/c (2 pills)
4. TAF / FTC / RAL / DRV/c (4 pills)
5. TAF / FTC / DTG / DRV/c (3 pills)
6. TAF/FTC/BIC (1 Pill)
7. TAF / FTC / DTG (2 pills)
8. Some other regimen

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Question

What regimen should I start when a patient returns after a long absence?

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Case 10

- 55 yo male returns after being "Lost to Follow Up" for 2 years
- Diagnosed 7 years ago with HIV infection
- Initial Rx: **TDF /FTC / RPV** (Tolerated well)
- **Initial:** HIV RNA 86,000 c/ml (wildtype virus)
  CD4 count 70 cells/ul
- **Status at last visit (2 years ago):**
  HIV RNA 26 c/ml / CD4 count 325 cells/ul
- Now returns and wants to re-engage in care
- Lab results pending

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ARS Question 12: What ARV therapy should you use now?

1. Same regimen as originally on
2. Start an InSTI-based regimen
3. Start a PI-based regimen
4. Wait for repeat resistance test, then choose regimen based on results
5. Some other answer

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Question

Should I stop abacavir in older patients?

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Case 11

- 62 yo male started on ARV Rx years ago (resistance history: wild type virus) **returns to you for care after 4 years** (Rx'd elsewhere)
- Has been through several regimens; now on ABC/ 3TC / DTG (fdc)
- **Now:** HIV RNA < 20 c/ml (persistently)
  CD4 560 cells/ul
  Cholesterol 180 mg/dl (HDL 52 / LDL 100)
  Creat 1.3 / eCrCl = 80 cc/min
- Smoker
- PMHx negative (No cardiac history)
- On atorvastatin and daily low-dose ASA

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ARS Question 13: Besides asking him to quit smoking, what would you do?

1. Continue his current ARV Rx
2. Change his ABC/3TC to TAF / FTC containing Rx
3. Change his ABC/3TC to DRV/rit (continue DTG)
4. Some other option

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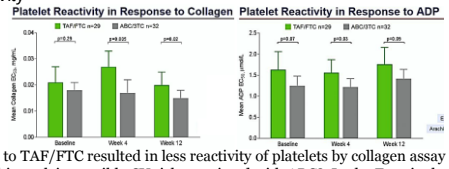
ABC → TAF – Effect on Platelets

- 61pts on ABC/3TC containing regimen randomized to continue or to switch to TAF/FTC. Platelet aggregation measured by platelet reactivity



- Switch to TAF/FTC resulted in less reactivity of platelets by collagen assay
- Does this explain possible CV risk associated with ABC? In the Framingham study ADP response was much more predictive for CVD than collagen response (MK Puurunen, JAHA 2018)

Mallon #677LB

Trial funded by Gilead Sciences, Inc

Conclusions

- ARV therapy should be initiated with an InSTI-based regimen (unless otherwise indicated), as close to time of Dx as possible
- Do not change Rx in setting of low-level viremia
- Use DTG, BIC, TAF and Cobi cautiously in women who are contemplating pregnancy
- M184V mutation does not have much impact on InSTI based Rx
- Weight gain is associated with initiation of ARV Rx, with more weight gain observed in InSTI regimens
- Standard PrEP is daily TDF/FTC, though newer approaches are being developed, including 2:1:1 episodic treatment

Question-and-Answer