

# **It's (not so) Complicated: Antiretroviral Therapy and Monitoring for Complications**

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# Objectives

- Identify common complications associated with antiretroviral therapy
- Discuss management options for adverse effects
- Review patient cases to demonstrate potential complications with antiretroviral therapy

# Complication vs. Side Effect

- Differentiating between complications of medications, side effects, and complications of HIV disease itself
  - **Complication:** a secondary disease or condition that develops in the course of a primary disease or condition and arises either as a result of it or from independent causes.
  - **Side effect:** an often harmful and unwanted effect of a drug or chemical that occurs along with the desired effect

# It's (not so) Complicated

- When antiretrovirals first came to market, for most, the benefit outweighed the risk of adverse effects and complications.
- People just 'dealt' with it, because these medications were literally life-saving. Or life-prolonging
- As recently as 2015, the guidelines still suggested that people could wait until their CD4 count dropped below 350-500 cells/mm<sup>3</sup> before starting ARVs.

# Current Recommendations

- Start comprehensive antiretroviral therapy (cART) in all HIV positive patients **regardless of CD4 count**
- First-line Recommended Regimens:
  1. *Dolutegravir/abacavir/lamivudine (Triumeq)*
  2. *Dolutegravir + tenofovir disoproxil fumarate/emtricitabine*
  3. *Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya)*
  4. *Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine (Stribild)*
  5. *Raltegravir + tenofovir disoproxil fumarate/emtricitabine*
  6. *Darunavir/ritonavir + tenofovir disoproxil fumarate/emtricitabine*

SINGLE TABLET REGIMENS

 **Atripla** efavirenz / emtricitabine / tenofovir, or EFV / FTC / TDF  
✓ DHHS ALTERNATIVE  
One tablet (500 mg efavirenz / 200 mg emtricitabine / 300 mg tenofovir), once daily. Take on an empty stomach, or with a light, low-fat snack.

 **Complera** rilpivirine / emtricitabine / tenofovir DF, or RPV / FTC / TDF  
✓ DHHS ALTERNATIVE ONLY IF HIV RNA < 100,000 C/ML AND CD4 > 200 CELLS/MM<sup>3</sup>  
One tablet (25 mg rilpivirine / 200 mg emtricitabine / 300 mg tenofovir), once daily. Take with a meal.

 **Genvoya** elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide, or EVG / COBI / ETC / TAF  
★ DHHS RECOMMENDED FOR FIRST-LINE USE  
One tablet (150 mg elvitegravir / 150 mg cobicistat / 200 mg emtricitabine / 10 mg tenofovir alafenamide), once daily with food.

 **Stribild** elvitegravir / cobicistat / emtricitabine / tenofovir DF, or EVG / COBI / ETC / TDF  
★ DHHS RECOMMENDED FOR FIRST-LINE USE  
One tablet (150 mg elvitegravir / 150 mg cobicistat / 200 mg emtricitabine / 300 mg tenofovir DF), once daily with food.

 **Triumeq** dolutegravir / abacavir / lamivudine, or DTG / ABC / 3TC  
★ DHHS RECOMMENDED FOR FIRST-LINE USE  
One tablet (50 mg dolutegravir / 600 mg abacavir / 300 mg lamivudine) once daily for people on HIV therapy for whom there is no known resistance to Triumeq. One additional 50 mg Triumeq tablet 12 hours apart if there is known viral resistance to Isentress or Vitekta (found in Germany).

 **Odefsey** rilpivirine / emtricitabine / tenofovir alafenamide, or RPV / FTC / TAF  
★ DHHS RATING NOT YET ESTABLISHED  
One tablet (25 mg rilpivirine / 200 mg emtricitabine / 300 mg tenofovir alafenamide), once daily, with a standard meal. Nutritional drinks, low-calorie protein shakes or products like Ensure, should be taken in place of a meal where you chew the food. Taken with...

INSTI INTEGRASE INHIBITORS

PI PROTEASE INHIBITORS

 **Isentress** raltegravir, or RAL  
★ DHHS RECOMMENDED FOR FIRST-LINE USE  
One 400 mg tablet, twice daily. No food restrictions (take with or without food).

 **Tivicay** dolutegravir, or DTG  
★ DHHS RECOMMENDED FOR FIRST-LINE USE  
One 50 mg tablet once daily for people on HIV therapy for the first time or treatment-experienced without previous INSTI resistance. When taken with certain ARVs, no food restrictions (take with or without food).

 **Evotaz** atazanavir / cobicistat  
✓ DHHS ALTERNATIVE  
One tablet (300 mg atazanavir / 150 mg cobicistat) once daily with food. Use in treatment-experienced patients depends on protease inhibitor drug resistance substitutions.

 **Kaletra** lopinavir / ritonavir, or LPV / r  
- DHHS OTHER  
Four tablets (200 mg lopinavir / 50 mg ritonavir), once daily if fewer than 3 lopinavir resistance mutations, or two 200 / 50 mg tablets, twice daily. Half-strength film-coated 100 mg lopinavir / 25 mg ritonavir tablet available. No food restrictions, but food may improve Norvir tolerability.

 **Norvir** ritonavir, or RTV  
★ USED ONLY AS A BOOSTER FOR OTHER DRUGS  
Used mostly for boosting, 100–200 mg, dosed once or twice daily with another PI. Must be taken with food.

 **Prezcobix** darunavir / cobicistat  
✓ DHHS ALTERNATIVE  
One tablet (800 mg darunavir / 150 mg cobicistat) once daily with food, in patients with no darunavir drug resistance.

 **Prezista** darunavir, or DRV  
★ DHHS RECOMMENDED FOR FIRST-LINE USE  
One 800 mg tablet with 100 mg Norvir or 150 mg Tybost, once daily for first-time therapy and treatment-experienced adults without Prezista-related resistance; or one 600 mg tablet plus 100 mg Norvir, twice daily for treatment-experienced people with Prezista-related resistance. Prezista must be taken with Norvir or Tybost. Take with food.

 **Reyataz** atazanavir sulfate, or ATV  
✓ DHHS ALTERNATIVE  
One 300 mg capsule plus 100 mg Norvir or 150 mg Tybost, once daily, or two 200 mg capsules (without boosting), once daily for treatment-naïve adults (see the Drug Guide for details). Take with food.

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MAJORITY RECOMMENDED

DHHS RATING

NO LONGER OR RARELY PRESCRIBED

NO LONGER OR RARELY PRESCRIBED

BRAND NAME NOT YET ESTABLISHED

DHHS RATING NOT YET ESTABLISHED

 **Tybost** cobicistat, or COBI  
✓ USED ONLY AS A BOOSTER FOR OTHER DRUGS  
Used only for boosting—not an antiretroviral. 150 mg once daily with food taken at the same time with either Prezista 800 mg or Reyataz 300 mg.

 **Emtriva** emtricitabine, or FTC  
★ DHHS RECOMMENDED FOR FIRST-LINE USE (A COMPONENT OF COMPLERA)  
One 200 mg capsule, once daily. No food restrictions (take with or without food).

 **EpiVir** lamivudine, or 3TC  
★ DHHS RECOMMENDED (CAN BE USED INTERCHANGEABLE)  
One 300 mg tablet, once daily, or one 150 mg tablet, twice daily. No food restrictions (take with or without food). Generic is available.

 **Epzicom** abacavir / lamivudine  
✓ DHHS ALTERNATIVE (UNLESS WITH TIVICAY)  
One tablet (600 mg abacavir / 300 mg lamivudine), once daily. No food restrictions (take with or without food).

 **Truvada** emtricitabine / tenofovir DF, or ETC / TDF  
★ DHHS RECOMMENDED FOR FIRST-LINE USE  
One tablet (200 mg emtricitabine / 300 mg tenofovir DF), once daily. No food restrictions (take with or without food).

 **Viread** tenofovir disoproxil fumarate  
★ DHHS RECOMMENDED (A COMPONENT OF TRUVADA)  
One 300 mg tablet, once daily. No food restrictions (take with or without food).

 **Ziagen** abacavir sulfate, or ABC  
✓ DHHS ALTERNATIVE (A COMPONENT OF EPZICOM) UNLESS IN TRIUMEQ  
Two 300 mg tablets, once daily; or one 300 mg tablet, twice daily. No food restrictions (take with or without food).

 **BRAND NAME NOT YET ESTABLISHED**  
emtricitabine / tenofovir alafenamide, or ETC / TAF  
DHHS RATING NOT YET ESTABLISHED  
Dose to be established.

MAJORITY RECOMMENDED

MAJORITY RECOMMENDED

DHHS RATING

NO LONGER OR RARELY PRESCRIBED

NO LONGER OR RARELY PRESCRIBED

BRAND NAME NOT YET ESTABLISHED

DHHS RATING NOT YET ESTABLISHED

 **Edurant** rilpivirine hydrochloride, or RPV  
✓ DHHS ALTERNATIVE WITH LIMITATIONS (A COMPONENT OF COMPLERA) AND ONLY WITH TRUVADA  
One 25 mg tablet, once daily. Take with food.

 **Intelence** etravirine, or ETR  
▽ ONLY FOR TREATMENT-EXPERIENCED INDIVIDUALS  
One 200 mg tablet, twice daily; or two 100 mg tablets, twice daily. Take with food.

 **Sustiva** efavirenz, or EFV  
✓ DHHS ALTERNATIVE WITH LIMITATIONS (A COMPONENT OF ATRIPLA)  
One 600 mg tablet or three 200 mg capsules, once daily. Take on an empty stomach, or may be taken with a light, low-fat snack.

 **Selzentry** maraviroc, or MVC  
▽ USED ONLY IN CERTAIN SITUATIONS  
150, 300, or 600 mg (available in 150 and 300 mg tablets), twice daily, depends on other medications used (see the POSITIVELY AWARE HIV Drug Guide for details). No food restrictions (take with or without food).

The following drugs are no longer or rarely prescribed, and appear only in the online version of the POSITIVELY AWARE HIV Drug Guide:

 <b>TPV 200</b> Aptivus tipranavir, or TPV	 <b>3TC/DF</b> Combivir lamivudine / zidovudine, or 3TC / AZT	 <b>IDV</b> Crixivan indinavir, or IDV
 <b>Fuzeon</b> enfuvirtide, T-20, or ENF	 <b>SQUV</b> Invirase sequinavir, or SQV	 <b>GLENCOR</b> Lexiva fosamprenavir calcium, or FPV
 <b>DLV</b> Rescriptor delavirdine, or DLV	 <b>AZT</b> Retrovir zidovudine, AZT, or ZDV	 <b>ABC/3TC/ATZ</b> Trizivir abacavir / lamivudine / zidovudine, or ABC / 3TC / AZT
 <b>ddI</b> Videx EC didanosine, or ddi	 <b>NFV</b> Virecept nelfinavir, or NFV	 <b>EVC</b> Vitekta elvitegravir, or EVG (Setim as a stand-alone drug.)
 <b>NVP</b> Viramune XR nevirapine, or NVP	 <b>RPV</b> Zerit stavudine, or d4T	

# Current Options

- Currently we have ~40 FDA approved medications for the management of HIV.
  - Six single tablet regimens (STL)
  - Many potential combinations
  - Compare to 2006: twenty-two FDA approved agents
- Only **SEVEN** are part of recommended first line regimens
- Great to have many options, but some options are better than others – all are efficacious
  - Many drugs that are no longer recommended had heavy side effect profiles. Fears of these prominent side effects still prevent some people from starting therapy

# Complications with 'older' antiretrovirals

- Neuropathy – indinavir (Crixivan)
- Lipoatrophy/lipodystrophy – stavudine (Zerit)
- Hepatotoxicity – nevirapine (Viramune)
- Dyslipidemia – protease inhibitors
- Bone marrow suppression – zidovudine
- Lactic acidosis – nucleoside reverse transcriptase inhibitors

## Stavudine

(greater than 10%)

CNS: headache 25-46%

Dermatologic: rash 18-30%

Gastrointestinal: nausea, vomiting, diarrhea 30-45%

Hepatic: hyperbilirubinemia 65-68%, increased AST 42-53%, increased ALT 40-50%

Neuromuscular: peripheral neuropathy 8-21%

## Raltegravir

(greater than 10%)

Hepatic: Increased ALT 1-11%

Other:

CNS: insomnia 4%

Hematologic: thrombocytopenia 1-3%

Neuromuscular: increased creatine phosphokinase 3-4%

# Complications and Side Effects Associated with all Antiretrovirals

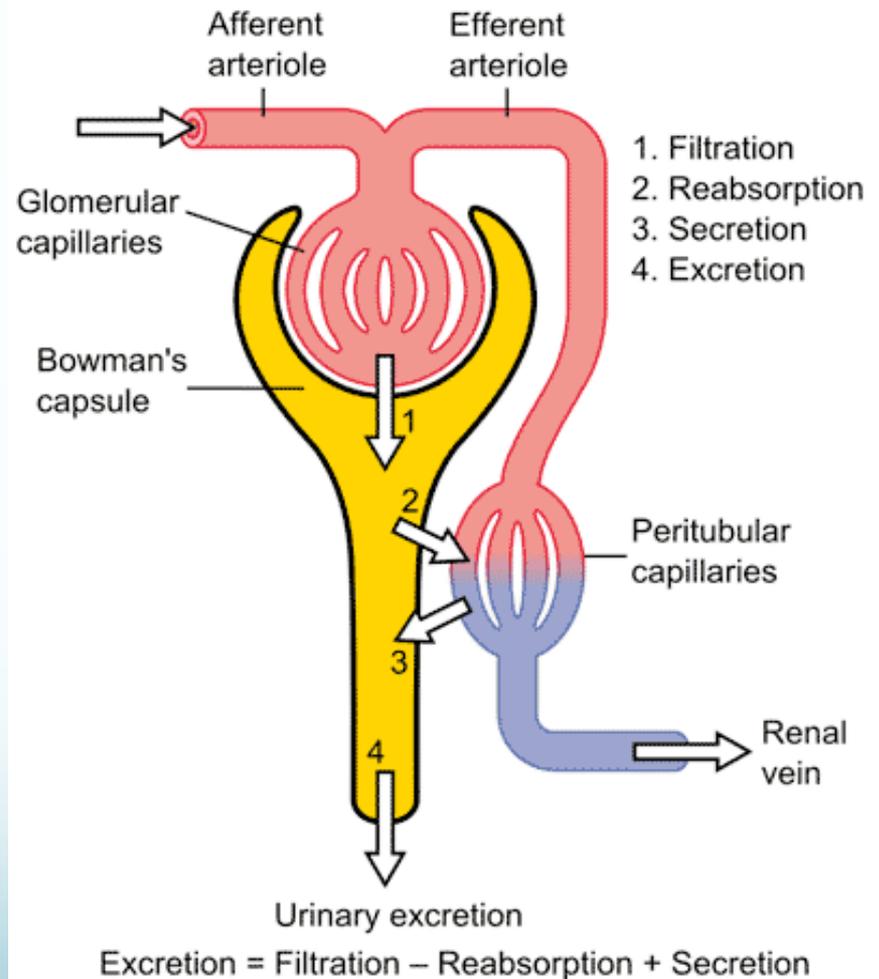
- Lipodystrophy/fat redistribution
- Decrease in bone mineral density
- Gastrointestinal issues
- Metabolic complications
  - Lipodystrophy
  - Dyslipidemia

# Patient Case 1

- Patient LA presents for her regular follow up in your clinic. She has been on Stribild (elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate) for about three years. Her most recent labs show that her viral load serum creatinine has increased from 0.9mg/dL to 1.15mg/dL. Urinalysis also shows proteinuria.
- You suspect one of her meds is currently altering her kidney function. Which of the following agents is likely responsible for this change?
- A. elvitegravir
- B. cobicistat
- C. emtricitabine
- D. tenofovir

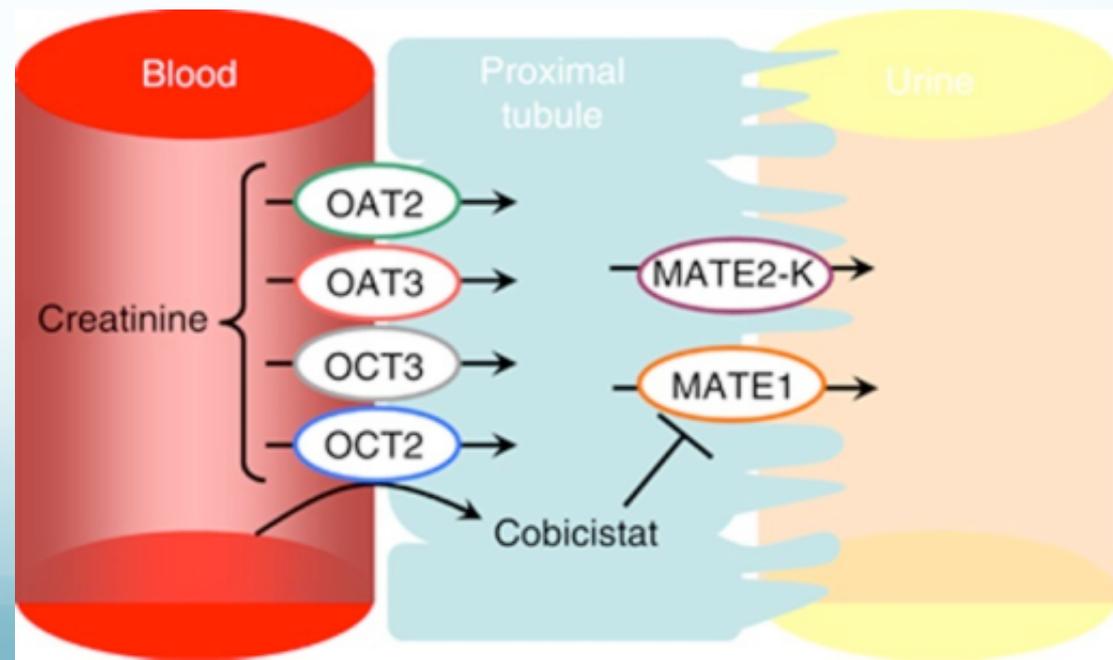
# Renal Complications

- Impact on serum creatinine (SCr) vs. actual change in kidney function/glomerular filtration
  - Remember, SCr is a **surrogate marker** to **estimate** creatinine clearance (CrCl) or estimated glomerular filtration rate (eGFR)



# Renal Complications - Cobicistat

- Pharmacokinetic booster with no antiretroviral activity, but a part of many cART regimens
- Inhibits renal tubular secretion of creatinine, thus increasing SCr level
- However, there is no impact on actual glomerular filtration rate.



# Renal Complications – Cobicistat

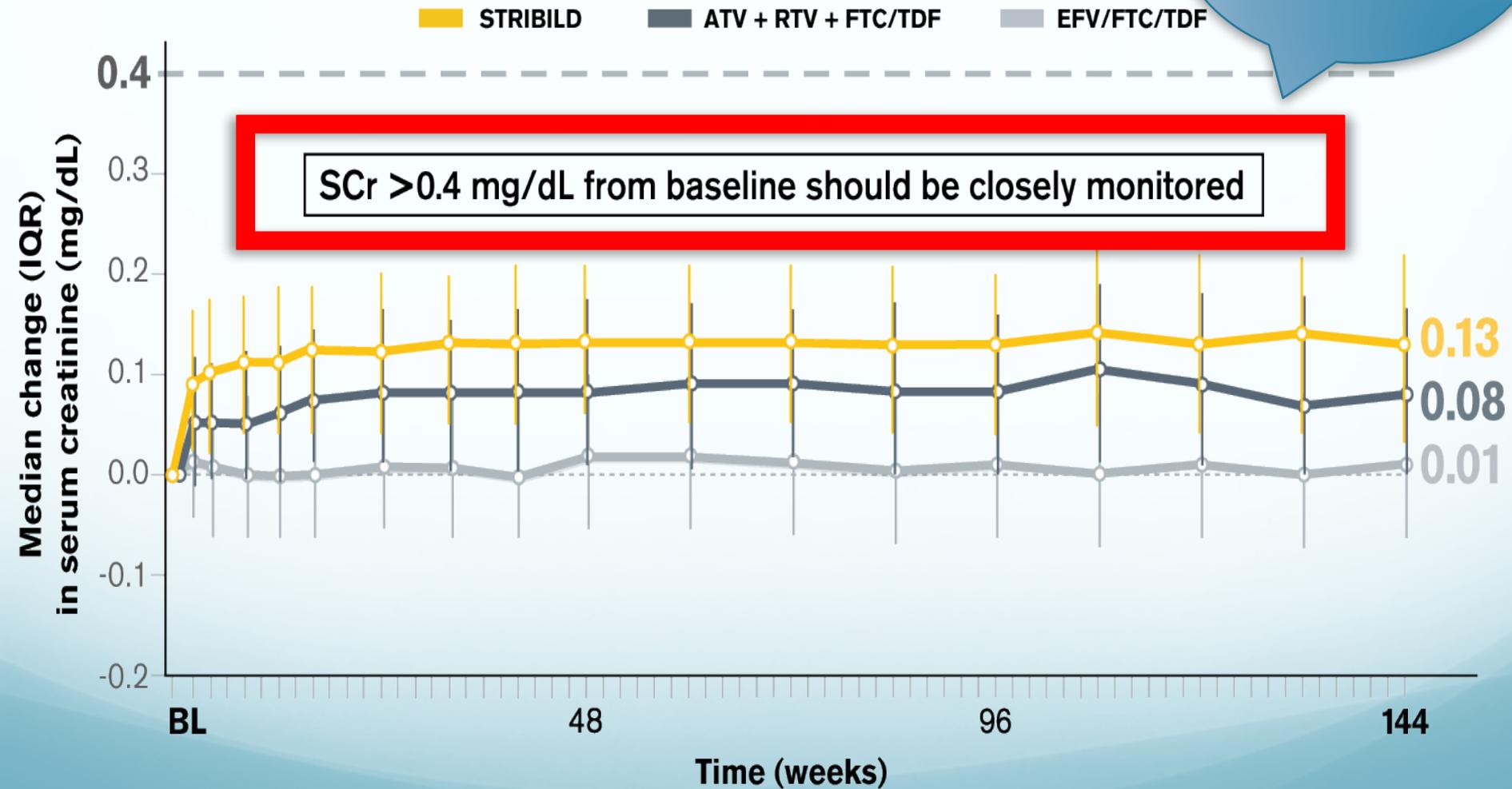
- Study by German et al. looked at the effects of ritonavir and cobicistat over 7 days.

	Ritonavir	Cobicistat
Mean change <b>SCr</b> @ day 7 from baseline	-0.11%	23.0%*
Mean change <b>SCr</b> @ day 14 from baseline (7d post d/c)	-3.76	4.11%*
Mean change in <b>actual GFR</b> @ day 7	1.8%	-5.0%
Mean change in <b>eGFR (Crockcroft-Gault)</b> @ day 7	1%	-17.5%

\* Denotes statistically significant

# Renal Complications – Cobicistat

Changes in SCr  
occur early,  
then stabilize



# Renal Complications – Cobicistat

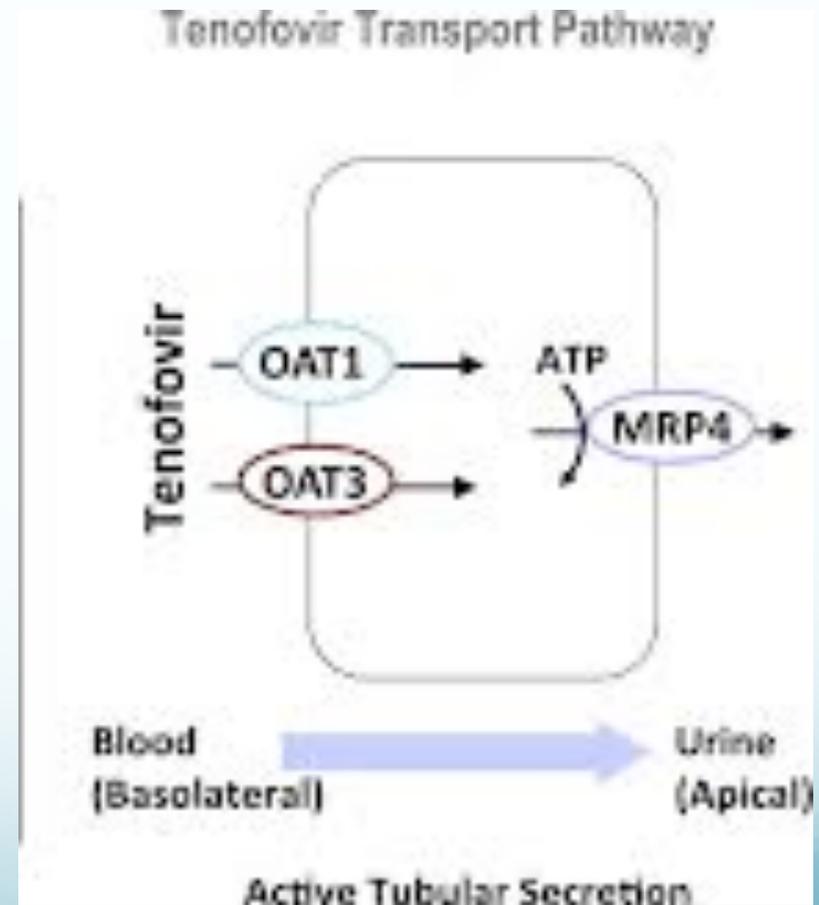
- Bottom Line
  - Increases in serum creatinine do not necessarily translate to impaired renal function
  - Changes in SCr occur early, then stabilize
- Management
  - Discontinue if serum creatinine continues to rise
  - Manage drug-drug interactions that increase levels of other nephrotoxic drugs (TDF!)
- Monitoring
  - Monitor SCr, specifically
  - Re-evaluate therapy if SCr increases more than the anticipated 0.4mg/dL baseline

# Renal Complications – Tenofovir disproxil fumerate

- Tenofovir disproxil fumerate (TDF) is a prodrug for tenofovir
  - Part of the majority of first line regimens
  - Active even in presence of M184V mutation
  - Also plays major role in, PrEP, PEP
- Most commonly used ARV, most complications?
  - Truvada, Atripla, Complera, Stribild

# Renal Complications – Tenofovir disoproxil fumarate

- Proposed mechanism
  - Build-up of intracellular tenofovir in the proximal tubules
  - Can be reversible (AKI) or permanent (CKD)

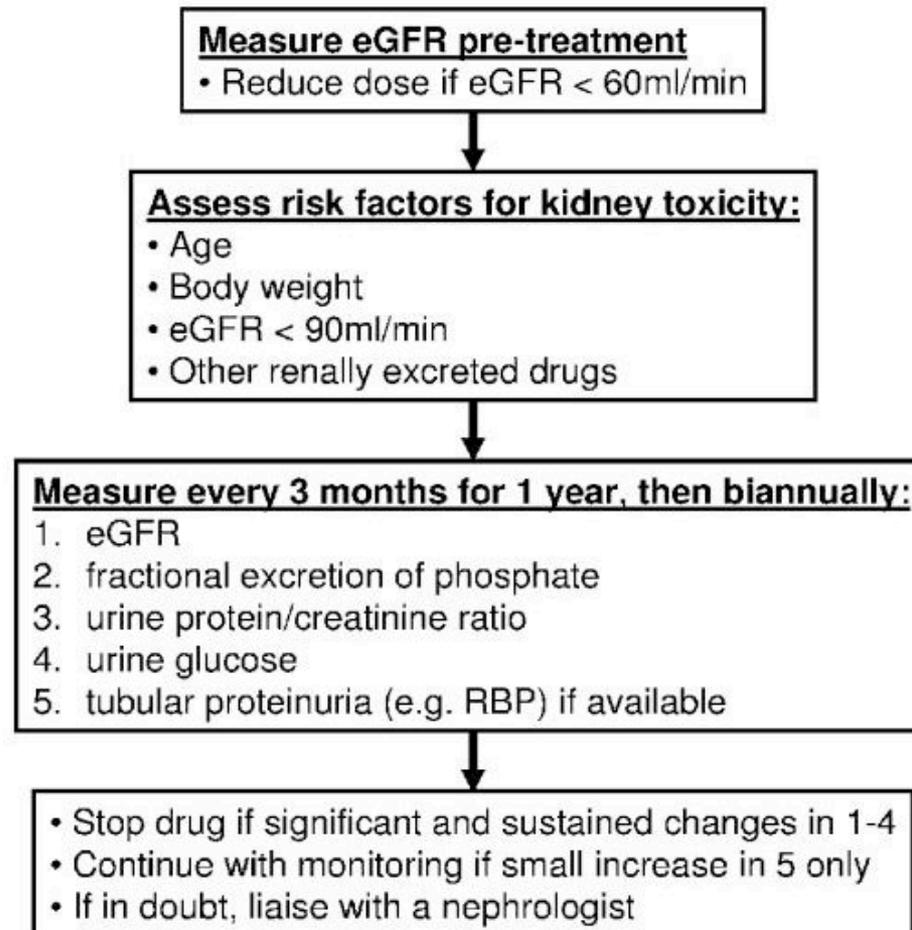


# Renal Complications – Tenofovir disproxil fumerate

- Fanconi's Syndrome
  - Rare
  - Proximal renal tubule dysfunction
  - Normal reabsorption of electrolytes impaired
  - Thus, spillage of electrolytes into urine
  - Objective findings
    - Increased urine protein:creatinine ratio (PCR)
    - Glucosuria with normal blood glucose
    - Hypophosphatemia

# Suggested Algorithm for Monitoring TDF Toxicity

Medscape



# Renal Complications – Tenofovir disoproxil fumarate

- Bottom line
  - TDF well known to cause actual nephrotoxicity
  - Close, regular monitoring
  - Despite risk, use of tenofovir does not need to be restricted in the general HIV population
- Management
  - Discontinue if SCr continues to rise
  - Decrease other nephrotoxic agents
  - Manage drug-drug interactions
  - Consider switch to TAF
  - Referral to nephrologist if prolonged impaired renal function
- Monitoring
  - Drug-drug interactions that may increase TDF concentrations
    - Cobicistat, ledipasvir (Harvoni component),
  - Serum creatinine, urinalysis (urine glucose, urine protein), serum phosphate (if suspected)

# Bone Mineral Density (BMD) loss

- Bone Mineral Density
  - Used to determine osteoporosis risk via dual-energy x-ray absorptiometry (DXA)
- BMD loss – a complication due to disease as well as antiretroviral therapy
  - Patients living with HIV more likely to have factors affecting BMD (CD4 cell count, higher baseline fasting glucose)
  - HIV disease itself is a risk factor
    - Osteoporosis prevalence may be as high as 3x higher than non infected patients

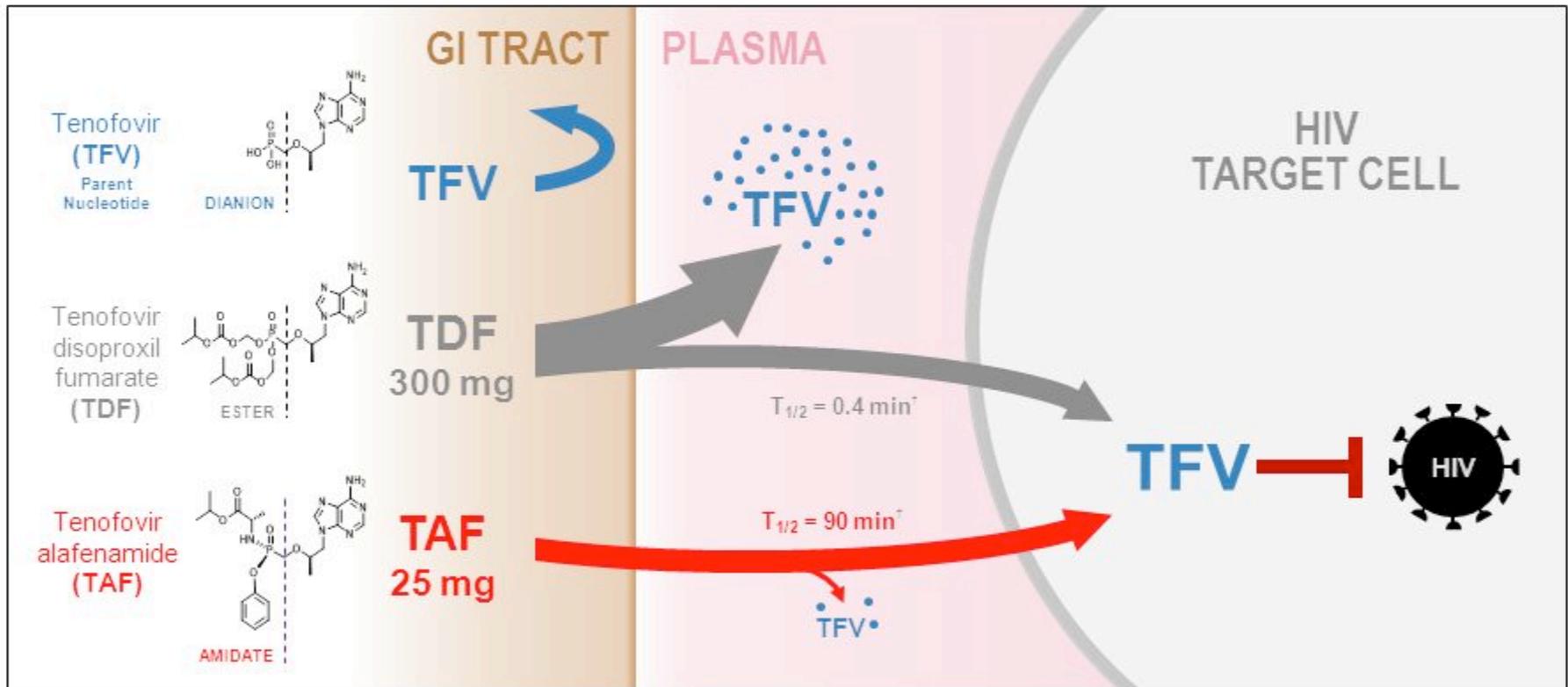
# Bone Mineral Density (BMD) loss

- All ARVs contribute to BMD loss
  - PI > NNRTI
  - TDF > ABC
- Brown, et al
  - ~2.5% BMD loss over 96 weeks. Not significant between ARVs.
- Grace et al.
  - Can be as high as >5% change in patients with other significant risk factors for osteoporosis

# Bone Mineral Density (BMD) loss

- Bottom line:
  - HIV disease itself can contribute to BMD loss
  - All ARVs contribute to BMD loss to some extent
- Management
  - Avoid TDF regimens in patients w/ history of osteoporosis/osteopenia
  - Bisphosphonates
  - Vitamin D supplementation - if level low
- Monitoring
  - Monitor for fragility fractures
  - Vitamin D levels
  - DXA – ideally, but not practically

# Tenofovir disoproxil (TDF) vs tenofovir alafenamide (TAF)



- **91% lower plasma TFV levels minimize renal and bone effects while maintaining high potency for suppressing HIV**

<sup>†</sup>  $T_{1/2}$  based on *in vitro* plasma data.

1. Lee W et. *Antimicrob Agents Chemo* 2005;49(5):1898-1906. 2. Birkus G et al. *Antimicrob Agents Chemo* 2007;51(2):543-550. 3. Babusis D, et al. *Mol Pharm* 2013;10(2):459-66. 4. Ruane P, et al. *J Acquir Immune Defic Syndr* 2013; 63:449-5. 5. Sax P, et al. *JAIDS* 2014. 2014;67(1):52-8. 6. Sax P, et al. *Lancet* 2015;385:2606-15.

# Tenofovir disproxil (TDF) vs tenofovir alafenamide (TAF)

**Genvoya™** 

elvitegravir 150mg/cobicistat 150mg/emtricitabine  
200mg/tenofovir alafenamide 10mg tablets

**Odefsey®** 

emtricitabine 200mg/rilpivirine 25mg/  
tenofovir alafenamide 25mg tablets

  
**Descovy®**  
emtricitabine 200mg/  
tenofovir alafenamide 25mg tablets

# Patient Case - 2

- A 60 year old man with a 10 year history of HIV presents to your clinic ready to start antiretroviral therapy for the first time. He is s/p MI two years ago. Other patient meds include: metoprolol 100mg, aspirin 81mg daily, and atorvastatin 40mg.
- Which of the following would be a reasonable option for his patient's ARV regimen? Patient has no major drug resistance mutations and is HLAB5701 Negative
  - A. Triumeq
  - B. Atripla
  - C. Tivicay + Truvada
  - D. Atazanavir/ritonavir + Truvada

# Cardiovascular Complications - Abacavir

- Abacavir – does it or doesn't it?
  - D.A.D Study (2008)
    - Association between 'recent' abacavir exposure and acute MI (HR 1.89)
    - Association was strong in those with underlying CV risk factors – bias?
  - No association: ACTG, French Hospital Database on HIV, US Veterans, etc.
  - Confusion!
    - US Veterans Cohort: three analysis – no association, statistically significant association with CV events
  - Meta Analysis
    - Also conflicted
  - No clear mechanism identified.
  - Again, may be a combination of antiretroviral complication plus complication of actual disease state.

# Cardiovascular Complications - Abacavir

**Table 2**

Main findings of prospective randomized clinical studies and meta-analysis of randomized clinical trials assessing the potential association between abacavir exposure and acute myocardial infarction in HIV-1 infected individuals.

Source	Type of analysis	Subjects included	Subjects exposed to ABC	AMI events	Type of exposure to ABC analysed	HR for ABC use (95% CI) <sup>a</sup>	AMI events/p/y	Additional analysis done	Era
GSK (Brothers et al., 2009)	Meta-analysis of randomized clinical trials	14,174	9502	27	Cumulative	0.52 (0.15–1.79)	1.9/1000	Absence of association in the whole RCT data set (0.813 [0.38 to 1.75])	1997–2006
STEAL Study (Martin et al., 2009)	Randomized clinical trial	357	179	4	Cumulative, 96 weeks	<b>8.33 (1.02–50)</b>	22/1000		2007–2008
Cruciani et al. (Cruciani et al., 2011)	Meta-analysis of randomized clinical trials	9233	4376	31	Cumulative	0.73 (0.39–1.35)	3.0/1000	Cardiovascular events RR 0.95 (95% CI 0.62–1.44); Overall mortality RR 1.20 (95% CI 0.63–2.27)	1996–2010
FDA (Ding et al., 2012)	Meta-analysis of randomized clinical trials	9868	5028	46	Cumulative	1.02 (0.56–1.83)	4.7/1000	Risk difference between ABC containing and non-ABC regimen is 0.008% (95% CI: –0.26%, 0.27%).	1996–2010

ABC: abacavir. P/y: patient/year. GSK: Glaxo Smith and Kline. FDA: Food and Drug Administration, US. CVE: Cerebrovascular events.

<sup>a</sup> Boldface highlights positive findings between abacavir exposure and AMI.

# Cardiovascular Complications - Abacavir

- Bottom line:
  - Overall, evidence is still conflicting on whether abacavir contributes significantly to CV events
- Management:
  - Consider avoiding abacavir in patients with a history of CV disease or CV events
- Monitoring:
  - Monitor for increased risk factors for CV disease or new development of

# Patient Case - 3

- Patient Mmis a 54yo male here for follow up 6 weeks after switching from Atripla to Triumeq. Today, he complains that he's become very grumpy lately and has been spending more time alone at home because he doesn't have the motivation to go spend time with his friends like he used to. He asks you to prescribe something 'for his mood'. What do you do?
  - A. Tell him the Atripla is still in his system, so he may be having residual side effects
  - B. Tell him to see a psychologist
  - C. Tell him that you will prescribe a low dose antidepressant
  - D. Tell him it there might be an association with dolutegravir, so he should discontinue the drug immediately.
  - E. None of the above

# Psychiatric Complications

- Efavarinez
  - Well documented, experienced by many patients, and they will tell you!
  - Vivid dreams, agitation, feeling 'hung-over' or 'groggy' the following morning
- Exacerbation of existing psychiatric disorders



# Psychiatric Complications

- Dolutegravir??
  - Kheloufi and colleagues report 4 cases of patients switching to dolutegravir and experiencing new onset psych symptoms or exacerbations. 2/4 pts did not have history of psychiatric disease.
    1. 56yo female; RAL → DTG d/t simplification;
      - After 1 week: dizziness, fatigue, 'feeling drunk'
      - Symptoms disappeared after d/c; no psych hx
    2. 43yo female; ATZ → DTG d/t metabolic adverse effects
      - After 1 month: headache, mentally depressed, irritability, angriness
      - Symptoms resolved 2 weeks post d/c
    3. 51yo female; ATZ → DTG d/t dyslipidemia
      - After a few days: feeling 'high'; 1 month: anxiety; 3 months: physician consulted d/t depressive syndrome and psychological distress.
      - Symptoms disappeared when switched back to atazanavir
    4. 64yo male; ATZ → DTG d/t dyslipidemia
      - After a few days: headaches, which resolved. 1 month: exacerbation of anxiodepressive symptoms with suicidal ideations
      - Symptoms resolved after a few months, DTG continued; Hx of severe psychological disease w/ no medications.

# Psychiatric Complications

- Bottom line
  - EFV has a well established high rate of significant psychiatric side effects
  - DTG may have associated psych effects not previously expected
- Management
  - EFV:
    - take on empty stomach to avoid increased concentrations with food
    - Avoid in patients with psychiatric history
    - Switch patient to first line recommended regimen
  - DTG:
    - Consider switch to alternative regimen
- Monitoring
  - Patient voiced complaints
  - Significant changes in mood or behavior
  - Monitor for drug-drug interactions

# Complications due to Patients

- Is resistance a complication of long-term ARV use?
- Complications due to inappropriately taking meds
  - missing doses
  - Not taking entire regimen (i.e. once daily vs twice daily or Truvada only)
  - Separating medication throughout day (i.e. Prezista in the morning, ritonavir at night, Truvada at night)
- Complications due to drug-drug interactions?
  - (not only due to patients!)
  - Stay tuned for next week's webinar!

# Questions?





*That's all Folks!*