Antiretroviral Therapy Initiation:
From Guidelines to Practice: ART 101
Medical Management of AIDS & Hepatitis
December 8, 2017
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• Research grant support from NIH, CDC, PEPFAR

Goals
• Working proficiency in selecting initial ART regimens
• Review DHHS first line & alternate regimens
  – Pros and cons, considerations/choices
  – Many updates from last year
• Will not focus on:
  – In-depth ART pharmacology
  – HIV drug resistance
  – 2-drug or Nucleoside-sparing regimens
  – ART for pediatric or pregnant patients
  – Drugs in development but not yet FDA approved
• 45 minutes... lots to cover!

US DHHS Guidelines: 1st Line Therapy

Recommended Initial Regimens for Most People with HIV
Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.

- ART & NRTIs
  - ATV/3TC/FTC (900mg/150mg/200mg) (or 400/60mg/200mg) or ATV/r/3TC/FTC (900mg/150mg/200mg)
  - ETV/3TC/FTC (900mg/200mg/200mg) or ETV/3TC/FTC (900mg/300mg/200mg)
  - RAL/FTC/FTC (400mg/300mg/200mg)
  - RAL/FTC/FTC (400mg/300mg/200mg) and boosted PI

Recommended Initial Regimens in Certain Clinical Situations
These regimens are effective and tolerable, but have some disadvantages when compared with the regimens listed above, or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred.

- ATV/3TC/FTC (900mg/150mg/200mg) or ATV/r/3TC/FTC (900mg/150mg/200mg)
- ETV/3TC/FTC (900mg/200mg/200mg)
- RAL/FTC/FTC (400mg/300mg/200mg)
- LPV/r plus 3TC: only PI/3TC regimen with 48-week RCT data in ART-naive patients

Adapted Footnotes:
• 3TC may be substituted for FTC, or vice versa
• TAF and TDF are two forms of tenofovir approved by the FDA. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.
• RAL can be given as 400 mg BID or 1200 mg (two 600-mg tablets) once daily.
• Several other NRTI-limiting treatment strategies are under investigation.
• LPV/r plus 3TC: only PI/3TC regimen with 48-week RCT data in ART-naive patients.
**U.S. DHHS Guideline Update:** October, 2017

**Initial Regimens for Most People**
- DTG/ABC/3TC
- DTG (cobi or DRV/RTV) + (TDF/FTC or TAF/FTC)
- EVG (cobi or TDF/FTC or TAF/FTC)

**Initial Regimens in Certain Clinical Situations**
- DTG/ABC/3TC
  - Only if HLB57-01 negative
- (DRV/cobi or DRV/RTV) + (TDF/FTC or TAF/FTC)
  - Only if HLB57 negative and VL<100,000
- (ATV/cobi or ATV/RTV) + (TDF/FTC or TAF/FTC)
  - Only if VL<100,000 & CD4+ >200
- RAL + (TDF/FTC or TAF/FTC)
  - Only if HLAB57 negative and VL<100,000

**FDA-Approved ARVs, 2017**

**NRTI (nucleoside analogs)**
- Tenofovir alafenamide (TAF)
- Tenofovir (TDF)
- Abacavir (ABC)
- Emtricitabine (FTC)
- Lamivudine (3TC)
- Didanosine (DDI)
- Zidovudine (ZDV)

**NNRTI (non-nucleosides)**
- Rilpivirine (RPV)
- Etravirine (ETR)
- Nevirapine (NVP)
- Delavirdine (DLV)

**Integrase Inhibitors**
- Dolutegravir (DTG)
- Elvitegravir (ETR)
- Raltegravir (RAL)

**Protease Inhibitors**
- Darunavir (DRV)
- Atazanavir (ATV)
- Ritonavir (RTV)
- Cobicistat (Cobi)
- Lopinavir (LPV)
- Fosamprenavir (FPV)
- Amprenavir (APV)
- Tipranavir (TPV)
- Nelfinavir (NFV)
- Saquinavir (SQV)
- Indinavir (IDV)

**CCR5 Inhibitors**
- Maraviroc (MVC)

**Fusion Inhibitors**
- Enfuvirtide (T-20)

**ARVs in Common Use, 2017**

**NRTI (nucleoside analogs)**
- Tenofovir alafenamide (TAF)
- Tenofovir (TDF)
- Abacavir (ABC)
- Emtricitabine (FTC)
- Lamivudine (3TC)

**NNRTI (non-nucleosides)**
- Rilpivirine (RPV)
- Etravirine (ETR)
- Nevirapine (NVP)
- Delavirdine (DLV)

**Integrase Inhibitors**
- Dolutegravir (DTG)
- Elvitegravir (ETR)
- Raltegravir (RAL)

**Basic Initial Regimen Composition**

Previously:
- 2x NRTI = TDF/FTC or ABC/3TC
- NNRTI = EFV or RPV
- PI

Currently:
- 2x NRTI = TDF/FTC or ABC/3TC
- INSTI
- or
- PI = r/ATV or r/DRV

Adapted from: US DHHS ART Guidelines – October 17, 2017 Update

FDA-Approved ARVs, 2017

NRTI (nucleoside analogs)
- Tenofovir alafenamide (TAF)
- Tenofovir (TDF)
- Abacavir (ABC)
- Emtricitabine (FTC)
- Lamivudine (3TC)
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- Rilpivirine (RPV)
- Etravirine (ETR)
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- Delavirdine (DLV)

Integrase Inhibitors
- Dolutegravir (DTG)
- Elvitegravir (ETR)
- Raltegravir (RAL)
NRTI’s: Tenofovir-based Meds

TDF/FTC (Truvada)

Renal Concerns
- Decrease in eGFR over time?

Bone Concerns
- Decrease in bone density?

- Concomitant increase risk of fracture?

TAF/FTC (Descovy)

Renal Profile
- better?

Bone Profile
- better?

Lipid Profile
- worse?

NRTI’s: TDF/FTC (Truvada)

TDF/FTC (Truvada): evidence supporting renal concerns?

- Slow, small magnitude decrement in eGFR over time?
- Small risk of proximal tubular toxicity/ Fanconi’s syndrome?

- A known low-level risk; forms the basis of monitoring

- Issues: controversial topic
  - observational study vs. RCT
  - baseline eGFR
  - low body weight
  - other renal risks
  - use of r/PI
  - other nephrotoxic meds

- Initial case reports 2002-2004

- Japanese cohort with larger decline in eGFR with TDF vs. ABC

- Laprise CID 2013

- A known low-level risk; forms the basis of monitoring

- Japanese cohort with larger decline in eGFR with TDF vs. ABC

- Laprise CID 2013

- Large meta-analysis including RCTs: small difference, perhaps 3-4 mL/min eGFR Cooper CID 2010

NRTI’s: TDF/FTC (Truvada)

TDF/FTC (Truvada): evidence for bone concerns?

- Decrement in bone density after ART initiation
- Then stabilization

- Clinical significance of a 2-4% loss of BMD unclear...

- No apparent evidence this translates to higher risk of fracture

- Spine BMD

- Hip BMD
**NRTI's: TAF/FTC (Descovy)**

**TAF** (tenofovir alafenamide)

- Oral pill
- Hydrolyzed to tenofovir in plasma
- Inverted to tenofovir- diphosphate inside cells
- Same nucleoside analogues as TDF
- Intracellular concentrations much higher

**Virologic non-inferiority to TDF/FTC (data through 144 weeks)**

- Sax PE et al., Lancet, 2015
- Wohl D et al., JAIDS, 2016
- Arribas J et al., JAIDS, 2017

**Evidence for improved renal profile?** (Data through 144 weeks)

- Less decline in eGFR:
  - Median drop in CrCl: -2.0 mL/min [ECF-TAF] vs. -7.5 mL/min [ECF-TDF] (p<0.001)
- Fewer discontinuations due to renal dysfunction:
  - 0 vs. 12 discontinuations [TAF vs. TDF]

**Evidence for improved bone profile?** (Data through 144 weeks)

- Less drop in BMD:
- Smaller rise in PTH

**Drug interactions**

- Rifamycins
  - Induce CYP3A4, P-gp, and BCRP
  - Inhibit OATP1B1, OATP1B3
  - Net effect of this unknown
  - Do not co-administer rifamycins with TAF

- TAF with cobicistat
  - TAF a substrate of CYP3A4, P-gp, OATP1B1, and OATP1B3
  - Cobi inhibits these boost TAF levels
  - Thus, TAF dose with cobi is same not 2.5mg

**Lipid profile**

- Lipid change from baseline to 144 weeks is worse in TAF vs. TDF:

<table>
<thead>
<tr>
<th></th>
<th>TAF</th>
<th>TDF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total chol.</td>
<td>↑11</td>
<td>↑13</td>
</tr>
<tr>
<td>HDL</td>
<td>↑6</td>
<td>↑2</td>
</tr>
<tr>
<td>LDL</td>
<td>↑15</td>
<td>↑8</td>
</tr>
<tr>
<td>TG</td>
<td>↑20</td>
<td>↑12</td>
</tr>
</tbody>
</table>

**Note:** TDF associated with favorable lipid profile.

- TAF is a move away from this favorable profile
### TAF and TDF Summary

<table>
<thead>
<tr>
<th>TDF/FTC (Truvada)</th>
<th>TAF/FTC (Descovy)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Renal Concerns</strong></td>
<td><strong>Bone Concerns</strong></td>
</tr>
<tr>
<td>Decrease in eGFR over time?</td>
<td>Decrease in bone density?</td>
</tr>
<tr>
<td>Risk of tubular toxicity?</td>
<td>Concomitant increase in risk of fracture?</td>
</tr>
</tbody>
</table>

Consider eGFR, proteinuria, osteoporosis, and need for rifamycins in this decision...

### NRTI’s: ABC/3TC (Epzicom)

#### ABC/3TC (Epzicom):

- **ABC Hypersensitivity**
  - Polymorphism of HLA-B57:01 allele
  - 4-8% of overall population positive; 2-4% among African Americans
  - ABC binds to HLA molecule, triggering HS reaction
  - Fully discriminative if positive: ABC contraindicated
  - If negative: ABC safe

- **Cardiovascular Concerns**
  - Enhanced platelet reactivity?
  - Platelet aggregation?
  - Promotes ischemic CV disease?
  - Theoretical basis for concern
  - Controversial

- **Basic biology**
  - HLA-B57-01 Testing
  - Database studies are equivocal
  - Do not clearly demonstrate MI risk

#### Issues: controversial topic
- observational studies vs. RCTs
- other CV risks: accounted for?
- risks from other ARVs?
- duration of follow-up?
- what outcomes assessed?

### NRTIs for Patients with HBV

- **For Hepatitis B positive patients:**
  - **TDF/FTC:**
    - 2 active agents: good choice
  - **TAF/FTC:**
    - 2 active agents
    - also FDA approved for HBV+ patients; good choice
  - **ABC/3TC:**
    - only the 3TC is active
    - if using ABC, typically combine with entecavir

### Integrase Inhibitors
**Integrase Inhibitor Overview**

**Dolutegravir (DTG)**
- Most potent, highly efficacious
- Higher genetic barrier to resistance
- 50mg QD dosing, no booster
- Need BID if using with EFV, rifampin
- Caution: DTG AUC decreased if eGFR<30...
- When use as ABC/3TC/DTG, only for eGFR>50...
- Increased AUC with low, moderate, high fat meal
- Decreased absorption when polyvalent cations given (Ca++, Mg++, Fe++)
- Space DTG 2h before or 6h after these
- Caution: boosts metformin levels
- Inhibits OCT2, inhibits tubular creatinine secretion, Cr 0.1 - 0.3
- Side effects → discontinuation initially thought to be <2-3% in first year
- Headache, insomnia increasingly recognized
- 15% (85/556) Amsterdam patients stopped DTG: 6% (sleep), 4% (GI), 4% (malaise), 3% (psychological) 2% joint/tendon/muscle, 2% neurologic
- Hypersensitivity/skin reactions uncommon (<1%)

**Integrase Inhibitors (cont’d)**

**Elvitegravir (EVG)**
- Well-tolerated, strong efficacy
- 150 mg QD dosing
- Requires cobicistat (50mg QD)
- Lower genetic barrier to resistance
- Hypersensitivity rare
- 1/866 patients had rash in EVG studies

**Raltegravir (RAL)**
- Very well-tolerated, good potency/efficacy
- 400mg BID dosing
- Can dose at 1200mg QD (noninferior to 400mg BID)
- No boosting required
- Lower genetic barrier to resistance
- Hypersensitivity reaction (rare, mild)
- Even rarer: DRESS syndrome

**Protease Inhibitor Overview**

**Darunavir (DRV/r)**
- Highest potency; fewer side effects than other PIs; well tolerated
- 800mg QD dosing (if no DRV mutations)
- 600mg BID dosing (when DRV mutations present)
- Side effects: overall low
- As with most PIs: GI side effects, skin rash (sulfa moiety) – usually self-limited, dyslipidemia, rare hepatotoxicity
- Advise take with food
- Unlike ATV: no hyperbilirubinemia; no spacing apart from H2-blockers; PPIs are ok
- Was in first line recommendations until latest update few weeks ago

**Protease Inhibitors**

Norvir: RTV 100
Prezista: DRV 800
RTV 100
Prezista: DRV 600
Protease Inhibitor Overview

- **Atazanavir (ATV/r)**
  - Good potency, generally well-tolerated, 300mg QD (+ RTV 100mg QD)
  - Least effect on lipids of PIs
  - ↑ bilirubin: sometimes cosmetic, sometimes beyond
  - GERD: in ART-naïve patients:
    - H2 blockers: give ATV 400QD 1h before or 1h after H2, give ATV300/RTV100 anytime
    - PPI: use omeprazole 20 or equivalent (maximum) 12h before ATV
  - Recommend take with food
  - Not in first line recommended list

  ![Protease Inhibitor Overview](image.png)

NNRTI's

NNRTI Overview

<table>
<thead>
<tr>
<th>NNRTI</th>
<th>Potency well established</th>
<th>Caution with depression</th>
<th>Lower efficacy when VL&gt;100K or CD4&lt;200</th>
<th>Requires 400 cal. meal</th>
<th>H2 blocker: give 12h before or 4h after RPV</th>
<th>PPI: avoid</th>
<th>Not in first line recommended list</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efavirenz</td>
<td>EDM</td>
<td>CNS side effects</td>
<td>1000mg QD</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>(EFV)</td>
<td></td>
<td>dreams</td>
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</tr>
<tr>
<td>Rilpivirine</td>
<td>POTENCY SIMILAR TO EFV</td>
<td>LIPID EFFECTS</td>
<td>250mg QD</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>(RPV)</td>
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</tr>
<tr>
<td>Etravirine</td>
<td>POTENCY SIMILAR TO EFV</td>
<td>BID DRUG (100mg BID)</td>
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<tr>
<td>(ETV)</td>
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Single Tablet Regimens

Sustiva: EFV 600
Edurant: RPV 25
Intelence: ETR 200 x2 (data support 400mg QD)
Not in first line recommended list
Single Tablet Regimens

**NRTI**
- Emtricitabine
- Lamivudine
- Abacavir
- Tenofovir
- Dolutegravir
- Rilpivirine
- Efavirenz

**NNRTI**
- Ritonavir

**INSTI**
- Elvitegravir

**Protease**
- Atazanavir
- Darunavir
- Cobicistat
- Raltegravir

**NRTI**
- Emtricitabine
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- Tenofovir
- Dolutegravir
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**NNRTI**
- Ritonavir

**INSTI**
- Elvitegravir

**Protease**
- Atazanavir
- Darunavir
- Cobicistat
- Raltegravir

**Cobicistat**

**Stribild**

**Genvoya**

**TAF**

*U.S. DHHS Guideline Update: October, 2017*

**Initial Regimens for Most People**

<table>
<thead>
<tr>
<th>Drug Combination</th>
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<td>DTG/ABC/3TC</td>
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<tr>
<td>DTG + TDF/FTC (or TAF/FTC)</td>
<td>Only HLA-B57 negative</td>
</tr>
<tr>
<td>EVG/cobi + (TDF/FTC or TAF/FTC)</td>
<td>Only HLA-B57 negative</td>
</tr>
<tr>
<td>RAL + (TDF/FTC or TAF/FTC)</td>
<td>Only HLA-B57 negative</td>
</tr>
<tr>
<td>EVG + (TDF/FTC or TAF/FTC)</td>
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**Initial Regimens in Certain Clinical Situations**

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<tr>
<td>EVG/cobi + DRV/RTV + ABC/cobi</td>
<td>Only HLA-B57 negative</td>
</tr>
<tr>
<td>ATV/cobi + (TDF/FTC or TAF/FTC)</td>
<td>Only HLA-B57 negative</td>
</tr>
<tr>
<td>ATV/cobi + RTV/ABC</td>
<td>Only HLA-B57 negative</td>
</tr>
<tr>
<td>EFV + (TDF/FTC or TAF/FTC)</td>
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Two organizational comments:
- DRV moved out of first line list in 2017...
- Guidelines don't emphasize TAF vs. TDF...
Case 1

- 51 year old man registering for care. VL = 41,000, CD4+ count = 682. Creatinine = 1.4, and eGFR = 55 mL/min. LDL = 68. HLAB57-01 is negative. No other medical problems. Which regimen(s) would you offer?

  - A) TDF/FTC (Truvada) + DTG
  - B) TAF/FTC (Descovy) + DTG
  - C) ABC/3TC/DTG (Triumeq)
  - D) TDF/FTC + RTV/DRV
  - E) EVG/cobi/TAF/FTC (Genvoya)
  - F) RAL + TAF/FTC

Case 2

- Same patient as Case 1, but lower eGFR:
- 51 year old man registering for care. VL = 41,000, CD4+ count = 682. Creatinine = 1.6, and eGFR = 31 mL/min. LDL = 68. HLAB57-01 is negative. No other medical problems. Which regimen would you offer?

  - A) TDF/FTC (Truvada) + DTG
  - B) TAF/FTC (Descovy) + DTG
  - C) ABC/3TC/DTG (Triumeq)
  - D) TDF/FTC + RTV/DRV
  - E) EVG/cobi/TAF/FTC (Genvoya)
  - F) RAL + TAF/FTC

Case 2

- 51 year old man registering for care. VL = 41,000, CD4+ count = 682. Creatinine = 1.4, and eGFR = 55 mL/min. LDL = 68. HLAB57-01 is negative. No other medical problems. Which regimen(s) would you offer?

  - A) TDF/FTC (Truvada) + DTG → eGFR >70: avoid TDF
  - B) TAF/FTC (Descovy) + DTG → Fine choice
  - C) ABC/3TC/DTG (Triumeq) → Fine choice
    - B57 negative: eligible, and no major CV concerns. Triumeq for eGFR>50.
  - D) TDF/FTC + RTV/DRV → eGFR <70: avoid RTV/PI + TDF combo
  - E) EVG/cobi/TAF/FTC (Genvoya) → eGFR <70: favor unboosted INSTI
  - F) RAL + TAF/FTC → Fine choice but prefer potency/genetic barrier of DTG
Case 3

- 48 y.o. man, newly diagnosed last month, VL 105,000, CD4+ count = 487. Has history of hyperlipidemia (LDL = 140, Total cholesterol = 221), smokes 10 cigarettes/day, and has HBA1c = 7.1%. BUN/creatinine 14/1.2, eGFR=73 mL/min, UA: 1+ protein. Which ART is optimal?
  
  - A) TDF/FTC (Truvada) + DTG
  - B) TAF/FTC (Descovy) + DTG
  - C) ABC/3TC/DTG (Triumeq)
  - D) TAF/FTC + RTV/DRV

Case 3

- 48 y.o. man, newly diagnosed, VL 105,000, CD4+ = 487. Has hyperlipidemia (LDL = 140, Total cholesterol = 221), smokes 10 cigarettes/day, HBA1c = 7.1%, BUN/creatinine 14/1.2, eGFR=73 mL/min, UA: 1+ protein. Which ART is optimal?
  
  - A) TDF/FTC (Truvada) + DTG
  - eGFR>70 is ok, but with 1+ proteinuria, would favor TAF over TDF
  - B) TAF/FTC (Descovy) + DTG
  - OK choice, eGFR>30, but already has proteinuria...
  - C) ABC/3TC/DTG (Triumeq)
  - OK choice, eGFR>50; but with CV risk factors (lipids/smoking/DM), balance CV risk with ABC vs. using TAF in patient with proteinuria
  - D) TAF/FTC + RTV/DRV
  - With cardiac and renal risk factors, avoid PI if possible

Case 4

- 34 y.o. woman, VL 23,000, CD4+ = 610. Has chronic HBV: HBsAg+ HBsAb+ HbcAb+ HBV DNA = 6M IU/mL. HLAB57-01 negative. eGFR=90. Which regimen(s) would you offer?
  
  - A) TDF/FTC (Truvada) + DTG
  - fine choice
  - B) TAF/FTC (Descovy) + DTG
  - fine choice
  - C) ABC/3TC/DTG (Triumeq)
  - 3TC alone: would add entecavir
  - D) TDF/FTC (Truvada) + RTV/DRV
  - OK, but prefer integrase > PI
  - E) ABC/3TC (Epzicom) + RTV/DRV
  - Need entecavir with 3TC, and also would prefer integrase > PI

Case 4

- 34 y.o. woman, VL 23,000, CD4+ = 610. Has chronic HBV: HBsAg+ HBsAb+ HbcAb+ HBV DNA+. HLAB57-01 negative. eGFR=90. Which regimen(s) would you offer?
  
  - A) TDF/FTC (Truvada) + DTG
  - fine choice
  - B) TAF/FTC (Descovy) + DTG
  - fine choice
  - C) ABC/3TC/DTG (Triumeq)
  - 3TC alone: would add entecavir
  - D) TDF/FTC (Truvada) + RTV/DRV
  - OK, but prefer integrase > PI
  - E) ABC/3TC (Epzicom) + RTV/DRV
  - Need entecavir with 3TC, and also would prefer integrase > PI
Case 5

- 57 y.o. woman, VL=14K, CD4=390. DM2: A1c=8.0%, takes metformin at maximum 875mg TID dose + glipizide 5mg BID, eGFR=90, UA with no protein. HLAB57 negative. Which ART regimen do you favor?
  
  A) TDF/FTC (Truvada) + DTG  
  B) TAF/FTC (Descovy) + DTG  
  C) ABC/3TC/DTG (Triumeq)  
  D) TDF/FTC/cobi/EVG (Stribild)  
  E) TAF/FTC + RAL  
  F) ABC/3TC + RAL

Potentially ok; potentially not
- DTG boosts metformin → would need close monitoring as already on max dose (but might be ok)
- If need to reduce metformin, might have to add 2nd med, or DM2 control may get worse

Same as choice A

Same as choice A

eGFR >70, no DDI* → fine choice
- but prefer to avoid cobicistat if RAL possible

eGFR >30, no DDI* → fine choice
- Balance your view of RAL vs. DTG against DM control

B57- negative, no DDI*, but this is listed as an "other" regimen: try to use something first line

**DDI** = drug-drug interaction*

Coming Soon & Relevant for ART Initiation

- **Bictegravir/TAF/FTC (50/25/200)**
  - **1490 Study**: B/F/TAF (n=327) vs. DTG + TAF/FTC (n=330)
    - Phase 3, double blind, PBO-matched study in ART naive adults; non-inferiority design (with -12% margin)
    - W48: VS 89% (B/F/TAF) vs. 93% (DTG + TAF/FTC), difference -3.5% (95% CI -7.9% to +1.0%, p=0.12)
  - **1489 Study**: B/F/TAF (n=316) vs. DTG/ABC/3TC (n=315)
    - Phase 3, double blind study in ART naive adults; non-inferiority design (with -2% margin)
    - W48: VS 92.4% (B/F/TAF) vs. 93% (Triumeq), difference -0.6% (95% CI -4.8% to +3.6%, p=0.78)
  - FDA announcement expected Feb. 2018

- **Darunavir/cobi/TAF/FTC (800/150/200)**
  - **AMBER Study**: Study (ART-naive adults, randomized to D/C/F/TAF (n=362) vs. DRV/cobi + TDF/FTC (n=363) to W48 (double blind phase III non-inferiority trial, -10% margin)
    - D/C/F/TAF: 91.4% VS at Week 48 vs. DRV/cobi + TDF/FTC: 88.4% VS (+2.7%, 95% CI -1.6% to +7.1%; met non-inferiority margin)
  - **EMERALD Study**: Ph. 3 switch study (in virally suppressed adults) also showed non-inferior maintenance of VS with D/C/F/TAF vs. control
  - NDA application to FDA made; action date uncertain

Coming Soon & Relevant for ART Initiation
Coming Soon & Relevant for ART Initiation

- **Dolutegravir + rilpivirine** (Juluca)
  - FDA approved 11/21/17 (two weeks ago) for maintenance for HIV therapy
  - **SWORD-1 & SWORD-2** Phase III switch studies: DTG/RPV 95% VS W4V8. Control: 95% VS, difference -0.2% (-3.0 to +2.5%)
  - Data on ART-naive patients not yet available

- **Dolutegravir + 3TC**
  - **GEMINI-1 & GEMINI-2**: ongoing Phase III studies in ART-naive individuals

Summary / Principles

- **Choosing the NRTI backbone:**
  - Consider TDF vs TAF
  - Assess eGFR, proteinuria, osteoporosis, importance of pill size
  - Consider ABC vs TDF/TAF
  - Need HLAB1 or test. Assess question/opinion of cardiac risk issues

- **Goal is to use INSTI in most patients unless other issues prevail**
  - Consider prior history, drug intolerance, side effect, desire for single-tablet regimen, drug interactions

- **Assess PI and NNRTI possibilities if needed:**
  - Consider dosing (QD vs. BID), desire for single-tablet regimen, psychiatric history, lipid profile, GL issues, renal status, likelihood of strong adherence/ genetic barrier
  - Assess baseline VL and CD4 count

- **Focus on DHHS recommended regimens**

References


References (2)


Thank You!

- Happy to take any questions

- For questions after the conference:
  - vivek.jain@ucsf.edu – please email me anytime