

# Can We Simplify This? Optimizing HIV Regimens for Pediatric HIV Patients

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April 10, 2019

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## Objectives

- 1) List preferred anti-retroviral regimens for pediatric patients according to the Department of Health and Human Services (DHHS) guidelines
- 2) Compare and contrast one-pill, once a day HIV regimens available to pediatric patients
- 3) Develop an optimized treatment plan for a pediatric patient with perinatal HIV including medication selection
- 4) Describe the role of tenofovir alafenamide (TAF) in pediatric HIV care
- 5) Identify barriers to adherence and ways to overcome them

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## Disclosure

- I have no relevant financial disclosures or conflicts of interest.
- The presentation may discuss the off-label use of medications.

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### Case 1

- CL is an 18 yo male with no significant past medical history who is sexually active with multiple partners (male and female). He does not regularly use protection. At the request of his pediatrician, he agrees to STI testing, which reveals that he is HIV positive.
- Should CL be treated?
  - A. Yes
  - B. No
  - C. I don't know

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### Question 1

- Which of the following regimens would be ideal to start in CL?
  - A. Efavirenz/Tenofovir Disoproxil Fumarate (TDF)/Emtricitabine (Atripla®)
  - B. Elvitegravir/Cobicistat/Tenofovir Disoproxil Fumarate/Emtricitabine (Stribild®)
  - C. Elvitegravir/Cobicistat/Tenofovir Alafenamide (TAF)/Emtricitabine (Genvoya®)
  - D. Bictegravir/Tenofovir Alafenamide/Emtricitabine (Biktarvy®)

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### Epidemiology

- In the United States, ~ 1,122,900 individuals were living with HIV
  - 60,300 youth living with HIV (51% without a diagnosis)
  - 21% of all new diagnoses are youth 13-24
- Worldwide
  - 36.9 million individuals living with HIV
    - 1.8 million children < 15 years
  - 21.7 million with access to anti-retroviral therapy
    - Only 52% of children < 15 years

HIV among youth. <https://www.cdc.gov/hiv/opa/young/youth/index.html>. Accessed 1 Feb 2019.  
 Global HIV & AIDS statistics — 2018 fact sheet. <http://www.unaids.org/en/resources/fact-sheet>. Accessed 1 Feb 2019.

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## Challenges to Prevention

- Inadequate Sex Education
  - Less than half of high schools teach all sexual health topics recommended by CDC
  - < 41% of schools require instruction on HIV prevention
- Risk Behaviors
  - Low rates of testing (only 10% of high school students)
  - Substance Use
  - Low rates of condom use
  - Number of partners
- High rates of STDs
- Feelings of isolation

HIV among youth: <https://www.cdc.gov/hiv/newsroom/youthissues/index.html> Accessed 1 Feb 2019  
 Global HIV & AIDS statistics — 2018 fact sheet: <http://www.unaids.org/en/resources/fact-sheet> Accessed 1 Feb 2019

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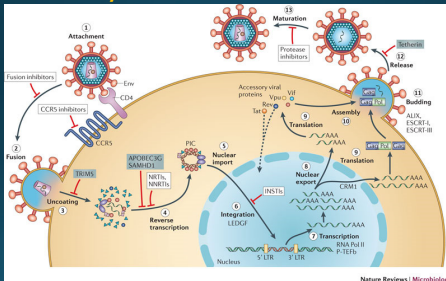
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## HIV Life Cycle



Nature Reviews | Microbiology | Post-Rev Microbiol. 2012; 10: 279-90.

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## Antiretroviral Classes

Nucleoside/tide Reverse Transcriptase Inhibitors (NRTIs)	Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)
Protease Inhibitors (PIs)	Integrase Strand Transferase Inhibitors (INSTIs)
Entry Inhibitors	Monoclonal Antibodies

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## Name that Medication!



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## Principles of Pediatric HIV Treatment

- All patients should be offered treatment
  - Highest urgency
    - < 1 year old (CHER trial)
    - CDC Stage 3 immunodeficiency or opportunistic illness
      - < 500 cells/ $\mu$ L for age 1-5 years
      - < 200 cells/ $\mu$ L for age  $\geq$  6 years
- Choose 3 medications from at least 2 different classes
  - Generally use a backbone of 2 NRTIs
  - Integrase inhibitors preferred 3<sup>rd</sup> agent

Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at <http://aidsinfo.nih.gov/contentfiles/lhvguidelines/childguidelines.pdf>. Accessed 1 Feb 2019.

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## Considerations for ART

- Availability of appropriate/palatable drug formulation
- Pharmacokinetic data
- Complexity of regimen
- Adverse Effects
- Long-term options
- Comorbidities
- Drug Interactions
- Ability of caregiver and child to adhere to regimen
- Previous medication regimens

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## Panel Recommendations

- Preferred
  - Data in children (or adults) shows optimal/durable efficacy
  - Acceptable toxicity
  - Ease of use
- Alternative
  - Data show efficacy
  - Distinct disadvantages compared to preferred regimens

Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at <http://aidsinfo.nih.gov/childrenlivingwithhiv/guidelines.cfm>. Accessed 4 Feb 2019.

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## Characteristics of an Ideal HIV Regimen

- Highly effective
- Small pill burden
  - Size
  - Number
- No drug-drug interactions
- Minimal drug-food interactions
- Minimal adverse effects
- High barrier to resistance

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## Preferred Regimens - < 12 years old

Age Group	Backbone Options	Third Agent
< 14 days	• Zidovudine + Emtricitabine or Lamivudine	• Nevirapine • Raltegravir
≥ 14 days – < 3 years	• Zidovudine + Emtricitabine or Lamivudine • Abacavir + Emtricitabine or Lamivudine (> 3 months old)	• Lopinavir/ritonavir • Raltegravir
≥ 3 years - < 6 years	• Zidovudine + Emtricitabine or Lamivudine • Abacavir + Emtricitabine or Lamivudine	• Raltegravir • Atazanavir + Ritonavir • Darunavir + Ritonavir (BID dosing)
≥ 6 years - < 12 years	• Abacavir + Emtricitabine or Lamivudine • Tenofovir Alafenamide/Emtricitabine	• Dolutegravir (Weight > 30 kg) • Atazanavir + Ritonavir

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### Considerations for Adolescent Patients

- Baseline resistance testing is imperative
  - Multiple studies showing relatively high rates of resistance
  - Sexual partners likely to be older and treatment-experienced
- Unique development stage
  - Show a strong desire to make own decisions
  - May show risk-taking behaviors
  - Self-image very important
  - Desire to fit in with peers
- Integrated approach to care is ideal
  - Inclusion of adolescent/youth clinic if possible

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Available at <http://aidsinfo.nih.gov/contentfiles/ltrguidelines/adolscychild/adolscychild.pdf>. Accessed 3 Feb 2019.

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### Sexual Maturity Rating (Tanner Stage)

- Stages 1-3
  - Follow pediatric guidelines
- Stages 4-5 (Postpubertal)
  - Follow adult guidelines
- May see delayed puberty in perinatal cases
- Neither SMR nor age can fully predict pharmacokinetics

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Available at <http://aidsinfo.nih.gov/contentfiles/ltrguidelines/adolscychild/adolscychild.pdf>. Accessed 3 Feb 2019.

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### Preferred Regimens - ≥ 12 years old and SMR 1-3

- Backbone
  - Emtricitabine/Tenofovir alafenamide
  - Abacavir + Lamivudine or Emtricitabine
- Third Agent
  - Atazanavir + Ritonavir
  - Dolutegravir (> 30 kg)
  - Elvitegravir (> 35 kg)
    - Available as combination only (Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide)
  - Darunavir + Ritonavir ONCE daily (> 40 kg)

Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at <http://aidsinfo.nih.gov/contentfiles/ltrguidelines/childguidelines.pdf>. Accessed 3 Feb 2019.

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### Preferred Regimens - ≥ 12 years old and SMR 4-5

- Dolutegravir/Abacavir/Lamivudine
- Dolutegravir + Tenofovir/Emtricitabine
- Raltegravir + Tenofovir/Emtricitabine
- Bictegravir/Tenofovir alafenamide/Emtricitabine (≥ 18 years)

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Available at <http://aidsinfo.nih.gov/contentfiles/livewith/adult/advguidelines.pdf>. Accessed 1 Feb 2019.

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### Antiretrovirals in Pediatrics

Class	Agents	Advantages	Disadvantages
Integrase Inhibitors	Dolutegravir Elvitegravir Raltegravir	Fewer drug-drug interactions Well-tolerated	Less pediatric data available Decreased absorption with polyvalent cations
Non-nucleoside Reverse Transcriptase Inhibitors	Efavirenz Nevirapine Rilpivirine	Long-half life Better toxicity profile compared to protease inhibitors Lower pill burden than protease inhibitors	Low barrier to resistance Rare but serious incidence of severe skin rash or hepatotoxicity Many drug interactions
Protease Inhibitors	Atazanavir Darunavir Lopinavir	High barrier to resistance Well-documented efficacy	Metabolic complications Drug Interactions Higher pill burden (all require boosting with ritonavir) Poor palatability of liquid

Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at <http://aidsinfo.nih.gov/contentfiles/livewith/pediatricguidelines.pdf>. Accessed 1 Feb 2019.

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### Notes on NRTIs

- Emtricitabine and Lamivudine are considered interchangeable
  - May incur resistance with M184V
  - Activity against Hepatitis B
- Abacavir
  - Requires genetic testing (HLA-B\*5701) prior to use
  - Twice daily dosing with liquid formulation
- Zidovudine
  - Alternative regimen when > 6 years old because of BID dosing
- Didanosine and Stavudine should NEVER be used

Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at <http://aidsinfo.nih.gov/contentfiles/livewith/pediatricguidelines.pdf>. Accessed 1 Feb 2019.

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## Single Tablet Regimens

- First-Line Regimens
  - Bictegravir/Emtricitabine/TAF (Biktarvy®)
  - Dolutegravir/Abacavir/Lamivudine (Triumeq®)
- Recommended in Certain Situations
  - Efavirenz/TDF/Emtricitabine (Atripla®)
  - Elvitegravir/Cobicistat/TAF/Emtricitabine (Genvoya®)
  - Elvitegravir/Cobicistat/TDF/Emtricitabine (Stribild®)
  - Rilpivirine/TAF/Emtricitabine (Odefsey®)
  - Rilpivirine/TDF/Emtricitabine (Complera®)
  - Darunavir/Cobicistat/TAF/Emtricitabine (Symtuza®)

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## Comparing Single-Tablet Regimens

Brand Name	Minimum Body Weight	Pill Size (mm x mm)	Food Requirement?
Atripla	40 kg	NA	Fasting
Complera	35 kg (≥ 12 years)	N/A	Food required
Odefsey	35 kg (≥ 12 years)	N/A	Food required
Biktarvy	≥ 18 years	15 x 8	No
Triumeq	40 kg	22 x 11	No
Genvoya	25 kg	19 x 8.5	Yes
Stribild	35 kg	N/A	Yes
Symtuza	40 kg (≥ 12 years)	N/A	Yes

Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV: Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at <http://aidsinfo.nih.gov/contentfiles/lhvsrch2018.pdf>. Accessed 1 Feb 2019.

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## Single Tablet Regimen Highlights

- Abacavir
  - Requires HLA-B\*5701 testing prior to use
- Dolutegravir
  - Careful consideration in women of child-bearing age
  - Possible neural tube defects
- Rilpivirine
  - Should not be used with high baseline viral load
  - Caution with psychiatric comorbidities
- Cobicistat-containing regimens
  - Numerous drug interactions

Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV: Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at <http://aidsinfo.nih.gov/contentfiles/lhvsrch2018.pdf>. Accessed 1 Feb 2019.

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### Question 1

- Which of the following regimens would be ideal to start in CL?
  - A. Efavirenz/Tenofovir Disoproxil Fumarate (TDF)/Emtricitabine (Atripla®)
  - B. Elvitegravir/Cobicistat/Tenofovir Disoproxil Fumarate/Emtricitabine (Stribild®)
  - C. Elvitegravir/Cobicistat/Tenofovir Alafenamide (TAF)/Emtricitabine (Genvoya®)
  - D. Bictegravir/Tenofovir Alafenamide/Emtricitabine (Biktarvy®)

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### Highlights

- Adolescents with newly diagnosed HIV likely can be treated with a single-tablet regimen
- The DHHS now lists multiple integrase inhibitor regimens as first-line for adolescents and adults
- Special consideration should be given to comorbidities and patient preferences

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### Case 2

- Pt JL is a 9 yo (wt 26.8 kg) with perinatal HIV infection and allergic rhinitis. Her current medication list is as follows:
  - Lamivudine 150 mg po BID (150 mg tablet)
  - Zidovudine 200 mg po BID (100 mg capsule)
  - Atazanavir 200 mg po daily (200 mg capsule)
  - Ritonavir 100 mg po daily (100 mg tablet)
  - Loratadine 10 mg po daily
- VL: < 20 copies/ml; CD4 934 cells/ $\mu$ L (35%)

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### Case 2 Discussion

- 1) How would you define this patient's current control?
- 2) What are her goals of therapy?
- 3) Is her current regimen preferred according to DHHS guidelines?
- 4) What is her current HIV pill burden?

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### Case 2 Question

- How often should viral load be assessed in JL?
- A. Monthly
- B. Every 3 months
- C. Every 6 months
- D. Annually

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### Vertical Transmission

- Major advances have improved rates of maternal-fetal transmission
  - Prior to interventions
    - 15-25% of formula-fed infants
    - 25-40% of breastfed infants
- ACT076: Landmark trial showing benefits of zidovudine
  - Reduced rates by ~70%
- Rates in countries with resources now < 1%

N Eng J Med. 2016. 374 (8):761-70.

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## Global Health



- Despite advances, vertical transmission remains
  - 220,000 cases in 2014
  - WHO's "optimistic" forecast is 1.94 million children with HIV worldwide in 2020
- Barriers
  - Lack of access to appropriate anti-retrovirals
  - Lack of breast-feeding alternatives
  - Lack of emphasis on post-partum HIV management
- Positives
  - Cuba as first country to be WHO validated for eliminating maternal-fetal transmission  
*N Eng J Med. 2016. 374 (8):761-70.*

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## Goals of Therapy – Pediatric HIV

- Preventing/reducing HIV morbidity and mortality
- Restoring or preserving immune function
- Maximally suppressing viral replication
- Preventing viral drug-resistance mutations
- Minimizing drug toxicity
- Maintaining normal growth and neurocognitive development
- Improving quality of life
- Preventing transmission to others

Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at <http://aidsinfo.nih.gov/contentfiles/lvguidelines/pediatricguidelines.pdf>. Accessed 1 Feb 2019.

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## Severity of Immunosuppression

Stage	< 1 year	1 - < 6 years	≥ 6 years
1	≥ 1500, ≥ 34	≥ 1000, ≥ 30	≥ 500, ≥ 26
2	750-1499, 26-33	500-999, 22-29	200-499, 14-25
3	< 750, < 26	< 500, < 22	< 200, < 14

Expressed as CD4 Count (cells/μL), CD4 %

Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at <http://aidsinfo.nih.gov/contentfiles/lvguidelines/pediatricguidelines.pdf>. Accessed 1 Feb 2019.

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### Monitoring the Pediatric Patient with HIV

Parameter	Baseline	1-2 weeks	2-4 weeks	Every 3-4 months	Every 6-12 months only
Adherence	X	X	X	X	
Viral Load	X		X	X	
CD4	X			X	
CBC with differential	X		X	X	
Complete Metabolic Panel	X		X	X	
Lipid Panel	X				X
Urinalysis	X				X

\*Resistance Testing and Hepatitis B Testing when changing therapies  
 Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at <http://aidsinfo.nih.gov/contentfiles/livewith/pediatricguidelines.pdf>. Accessed 1 Feb 2019.

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### Difficulties in Pediatric HIV Treatment

- Poor palatability
  - Bitter taste
- Regimen complexity
  - Large pill burden
  - Measurement difficulties with liquid
- Swallowing
  - Studies finding caregivers choosing alternatives (e.g. crushing tablets, opening capsules)
- Storage and Transportation
  - Cold-chain storage difficult in resource limited setting

AIDS Res Ther. 2016;2016:1654938.

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### Liquid Formulations

- Available as a liquid
  - Abacavir
  - Darunavir
  - Emtricitabine
  - Lamivudine
  - Lopinavir/ritonavir
  - Nevirapine
  - Ritonavir
  - Zidovudine
- Available in Packets/Oral Granules
  - Atazanavir
  - Raltegravir
  - Tenofovir Disoproxil Fumarate

Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at <http://aidsinfo.nih.gov/contentfiles/livewith/pediatricguidelines.pdf>. Accessed 1 Feb 2019.

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## Discussion

Would you switch JL's current regimen?

Age Group	Backbone Options	Third Agent
≥ 6 years - < 12 years	<ul style="list-style-type: none"> <li>• Abacavir + Emtricitabine or Lamivudine</li> <li>• Tenofovir Alafenamide/Emtricitabine</li> </ul>	<ul style="list-style-type: none"> <li>• Dolutegravir (Weight &gt; 30 kg)</li> <li>• Atazanavir + Ritonavir</li> </ul>

Brand Name	Minimum Body Weight	Pill Size (mm x mm)	Food Requirement?
Genvoya	25 kg	19 x 8.5	Yes

A. Yes  
 B. No  
 C. I don't know

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## Case 2

- Pt JL is a 9 yo (wt 26.8 kg) with perinatal HIV infection and allergic rhinitis. Her current medication list is as follows:
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## Question

- You are the pharmacist working with JL's team and assisting in her transition to a new regimen. You plan on calling JL's family to check-in regarding adherence as her next visit is not until next month. When would be the best time to call JL?
  - A. 1 day
  - B. 3 days
  - C. 10 days
  - D. 21 days

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## Case 2 Highlights

- Pediatric HIV regimens are often complex and require critical evaluation of dosing formulations, patient weight, and pill burden
- Adherence should be checked frequently
- Visits should occur with the patient every 3-4 months to assess adherence, viral load, and CD4 count

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## Case 3

• GM is a 17 yo female with perinatal HIV who has been well-controlled on elvitegravir/cobicistat/TDF/emtricitabine (Stribild®). She has been on this regimen since the age of 12 and has excellent adherence. She does not have any other chronic conditions. Her provider is hoping to change her regimen.

Would you change GM's regimen?

- A. Yes
- B. No
- C. I Don't Know

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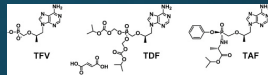
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## Tenofovir



- Nucleoside reverse transcriptase inhibitor (NRTI)
- Pro-drug converted to tenofovir which is phosphorylated within cells to tenofovir-diphosphate (TFV-DP)
- Two approved salt formulations
  - Tenofovir disoproxil fumarate (TDF)
    - Metabolized to tenofovir in PLASMA
  - Tenofovir alafenamide (TAF)
    - Metabolized to tenofovir in CELLS

*Medicine. 2016; 95 (4): e5146.*

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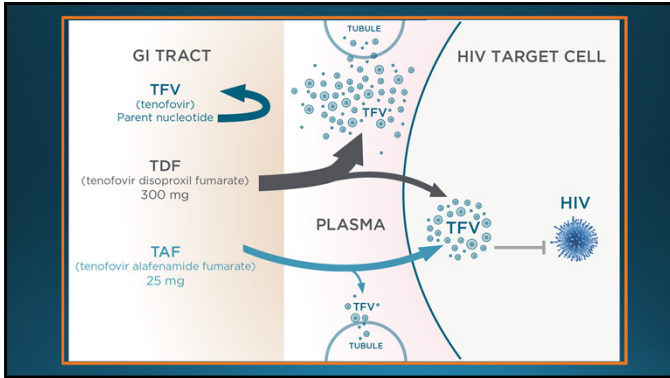
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### Tenofovir Alafenamide (TAF)

- Proposed benefits
  - Less decline in bone mineral density (BMD)
  - More favorable in regards to renal toxicity
  - Equivalent efficacy
- Proposed disadvantages
  - Less favorable effect on lipids

*Medicine. 2016; 95 (41): e5146.*

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### TDF v. TAF

- Meta-analysis including 6 randomized controlled trials
  - 3269 patients in TAF group
  - 2649 patients in TDF group
  - Two phase 2 trials; Four phase 3 trials
  - Four treatment naïve trials; Two therapy change trials
  - Adult patients
- Pediatric trials of TAF are small and have not directly compared TAF with TDF

*Medicine. 2016; 95 (41): e5146.*

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### TDF v. TAF: Efficacy

Effect	Patient Group	TAF group	TDF group	Relative Risk	95% Confidence Interval
Viral Suppression	All Patients	93.6%	91.2%	1.02	1.01-1.04
	Treatment Naïve	90.2%	89.5%	1.01	0.99-1.04
	Treatment Experienced	96.4%	93.1%	1.03	1.01-1.06
Rates of Resistance	All Patients	0.8%	0.72%	1.03	0.58-1.83
	Treatment Naïve	0.72%	0.65%	1.08	0.52-2.24
	Treatment Experienced	0.93%	0.87%	0.96	0.38-2.39

*Medicine. 2016; 95 (41): e5146.*

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### TDF v. TAF: Lipid Profile

Effect	Patient Group	TAF group	TDF group	P-Value
Change in Total Cholesterol (mg/dL)	Treatment Naïve	+33	+12	0.014
	Treatment Experienced	+17	+1.5	0.036
Change in Low-Density Lipoprotein (LDL), (mg/dL)	Treatment Naïve	+20	+4.5	0.124
	Treatment Experienced	+11	+1	0.109

*Medicine. 2016; 95 (41): e5146.*

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### TDF v. TAF: Bone Mineral Density

Effect	Patient Group	TAF group	TDF group	P-Value
% Change in BMD from baseline (Hip)	Treatment Naïve	-0.7%	-3.25%	0.005
	Treatment Experienced	+1.3%	-0.25%	0.029
% Change in BMD from Baseline (Spine)	Treatment Naïve	-1.29%	-3.28%	0.002
	Treatment Experienced	+1.54%	-0.32%	0.036

*Medicine. 2016; 95 (41): e5146.*

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### TDF v. TAF: Renal Function

Effect	Patient Group	TAF group	TDF group	P-Value
Change in eGFR <sub>CG</sub> from baseline (ml/min)	Treatment Naïve	-4.93	-10.63	0.007
	Treatment Experienced	+4.8	-0.45	0.392
Change in serum creatinine concentration (mg/dL)	Treatment Naïve	+0.065	+0.095	0.051
	Treatment Experienced	-0.24	+1.43	0.376

*Medicine. 2016; 95 (41): e5146.*

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### Application: TAF v. TDF

- General recommendation
  - SWITCH patient if amenable
  - Avoid risk of long-term toxicity
  
- Where does this not apply?
  - Pre-exposure prophylaxis (PREP)
  - Post-exposure prophylaxis (PEP)

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### Discussion

- What might be some reasons to consider switching a patient's regimen?

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### When to switch

- Resistance suspected
  - Increase in viral load
  - Resistance testing should be done
- Avoiding drug-drug interactions
- Preventing long-term toxicities
- Promote better adherence

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### Case 3

• GM is a 17 yo female with perinatal HIV who has been well-controlled on elvitegravir/cobicistat/TDF/emtricitabine (Stribild®). She has been on this regimen since the age of 12 and has excellent adherence. She does not have any other chronic conditions. Her provider is hoping to change her regimen.

Would you change GM's regimen?  
 A. Yes  
 B. No  
 C. I Don't Know

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### Case 4

• JR is a 13 yo male (wt = 42 kg) with perinatally acquired HIV and asthma who is currently on the following medications:  
 Atazanavir 400 mg po daily (2 x 200 mg capsules)  
 Ritonavir 100 mg po daily (1 x 100 mg tablet)  
 Emtricitabine/Tenofovir alafenamide 200 mg/25 mg po daily  
 Fluticasone 110 mcg/act, 1 puff BID

JR currently misses at least 2 doses of his anti-retrovirals per week. His HIV control has remained, but his parents are concerned about his long-term management and have questions about what can be done to help maintain his health.

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## Adherence in HIV Care

- Goal adherence: At least 95% of medication doses taken
  - If adherence is only 80-95%
    - 61% treatment failure
  - If adherence < 80%
    - 80% treatment failure
- Partial adherence is actually worse than complete non-adherence

UNAIDS/WHO AIDS epidemic update, Geneva: UNAIDS, World Health Organization, 2011.

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## Adherence Concerns in Adolescents

- Denial or fear of the diagnosis
- Misinformation
- Poor trust in medical system
- Fear of anti-retroviral medications
- Low self-esteem
- Unstructured lifestyle
- Mood disorders/mental illness
- Lack of familial support
- Inconsistent access to care/insurance
- Fear of diagnosis disclosure if using parental insurance

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Available at <https://aidsinfo.nih.gov/locations/about/aidsinfo/2015/adult-and-adolescent-guidelines-for-the-use-of-antiretroviral-agents-in-adults-and-adolescents-living-with-hiv>. Accessed 4 Feb 2019.

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## Methods to improve adherence

- Reminder Systems (should be low-key, yet attractive to the teen)
  - Phone apps
  - Times
  - Pill boxes
- Education
  - Goals of care: Need to balance side effects of treatment with seemingly asymptomatic disease
- Programs should be user-friendly and avoid stigma

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Available at <https://aidsinfo.nih.gov/locations/about/aidsinfo/2015/adult-and-adolescent-guidelines-for-the-use-of-antiretroviral-agents-in-adults-and-adolescents-living-with-hiv>. Accessed 4 Feb 2019.

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### mHealth (Mobile Health)

- Pilot studies with cell phones have suggested feasibility and acceptability with improvements in self-reported adherence
  - Limitations
    - Small numbers of patients
    - High numbers of dropouts
    - Unclear durability
- Scale-It-Up program
  - Trial of adherence using SMART design (adaptive)
  - Cell phone support or Text messaging service
  - Results in 2020

AIDS Patient Care STDS. 2015 July;29(6):338-45.  
JMR Res Protoc. 2018 Dec 20;7(12):e11183.

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### Strategies for Adolescents

- Deferring ART
  - Should be short-term in nature
  - Work on aggressively identifying and solving adherence issues
  - Coordinate with teen/adolescent health and mental health services
- Adherence testing period
  - Using a surrogate tablet to build up medication-taking skills (e.g. multivitamin)
- Avoid regimens with low resistance barriers

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Available at <https://aidsinfo.nih.gov/ContentFiles/ARTGLS/AdultsAndAdolescents.pdf>. Accessed 1 Feb 2019.

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### Case 4

- Which of the following regimens would be the best option for JR moving forward?
  - Dolutegravir/Abacavir/Lamivudine
  - Atazanavir+Ritonavir+Emtricitabine/Tenofovir Alafenamide
  - Darunavir+Ritonavir+Emtricitabine/Tenofovir Alafenamide
  - Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide

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### Transitioning the Pediatric HIV Patient

- Difficulties
  - Less integrated services
  - Insurance/access concerns
  - Concerns for confidentiality
  - Larger, intimidating clinics
- Interventions
  - Individualized transition plan
  - Optimizing provider communication
  - Assist teens in development of life skills
  - Incorporating family planning into clinical care

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### Summary

- Pediatric HIV remains a global health concern
- New regimens facilitate better adherence with fewer side effects
- Additional studies are still needed to optimize HIV treatment in younger patients

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### Can We Simplify This? Optimizing HIV Regimens for Pediatric HIV Patients

Kevin Patrick Lonabaugh, PharmD, BCACP AAHIVP, AE-C  
Clinical Pharmacist – Pediatric Ambulatory Care  
University of Virginia Health System  
April 10, 2019

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