

CLINICAL PEARLS OF NEW HIV MEDICATIONS



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PHARMACIST OBJECTIVES

- At the end of this presentation pharmacists will be able to:
- Describe dosing, side effects, and toxicities of new HIV medications.
- Counsel patients effectively when incorporating new HIV medications into a treatment regimen.



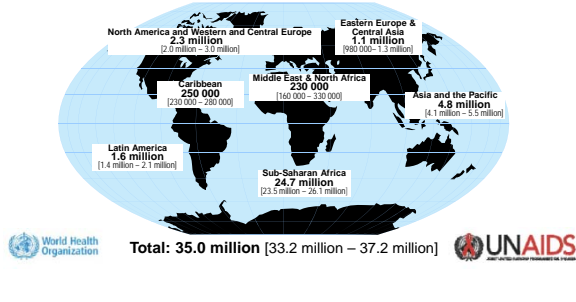
TECHNICIAN OBJECTIVES

- At the end of this presentation pharmacy technicians will be able to:
- Describe dosing, side effects, and toxicities of new HIV medications.
- Review how patients can be effectively counseled when incorporating new HIV medications into a treatment regimen.



GLOBAL PERSPECTIVE

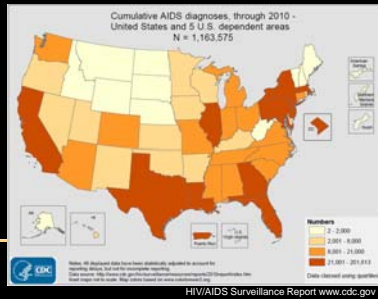
Adults and children estimated to be living with HIV | 2013



USA HIV/AIDS

CUMMULATIVE AIDS CASES REPORTED TO CDC

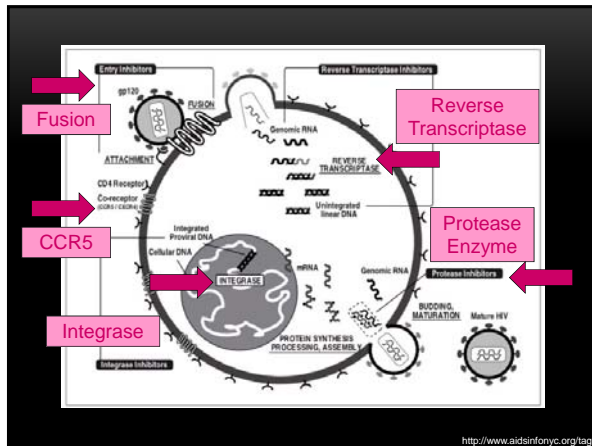
- 1) New York
- 2) California
- 3) Florida
- 4) Texas
- 5) New Jersey
- 6) Georgia
- 7) Illinois
- 8) Pennsylvania
- 9) Maryland
- 10) Puerto Rico



USA HIV/AIDS


- ~1.2 million persons aged ≥ 13 living with HIV in USA
- ~50,000 new HIV infections annually in USA
- Older patients, women, and those from racial / ethnic minorities are increasingly being impacted
 - Race – 72% from ethnic minority with 46% African American and 21% Hispanic
 - Age – 18% new infections in persons ≥ 50 years
- Life expectancy of an HIV patient diagnosed prior to decline in immune function is no different than a patient without HIV making HIV a treatable chronic medical condition

CDC HIV Statistics Overview 2013 www.cdc.gov



NRTIS

- Nucleoside Reverse Transcriptase Inhibitors
- 9 Drugs
- Mechanism of Action:
 - structurally similar to DNA bases (adenine, guanine, cytosine, and thymine) must be phosphorylated intracellularly to triphosphate, incorporates itself into the viral DNA via viral RNA dependent DNA polymerase (reverse transcriptase), producing viral DNA that is incorrect and incapable of infecting other cells



TENOFIVIR

- Parent compound adefovir (Hepsera®) too nephrotoxic at doses needed for HIV treatment low dose 10mg licensed for Hepatitis B (HBV)
- Reengineered as tenofovir (Viread®) FDA approved in 2001 for HIV
- Gilead did not pursue FDA approval for tenofovir for HBV until 2008 when patent on adefovir was expiring
- Other indications Gilead pursued for tenofovir in combination with emtricitabine (Truvada®) was prevention of HIV infection or (PrEP) pre-exposure prophylaxis in HIV negative individuals

Viread® Package Insert March 2010



TENOFOVIR



- Nucleotide analog contains 1st of 3 phosphorylations needed for antiretroviral activity creates a more metabolically active compound
- Tenofovir is renally eliminated from the body
 - glomerular filtration & active tubular secretion
- Fanconi syndrome resulting damage by tenofovir
 - acute renal failure, increased urine phosphate excretion
- Dose reduction for CrCL <50mL/min
- Decreases bone mineral density as body tries to compensate for urinary phosphate losses by breaking down bone to maintain serum phosphate levels
 - cases of osteomalacia have been reported was not FDA approved for children <18 until March 2010

Viread® Package Insert March 2010

TAF – NEW TENOFOVIR

- Estimated 84% of US HIV patients take tenofovir in some form of ART regimen both as an individual agent and in combination products recommended preferred agent in National DHHS HIV Guidelines
- Gilead reengineered tenofovir to reduce toxicities
- Tenofovir alafenamide fumarate (TAF) (formerly GS-7340) is a novel prodrug of tenofovir
- Greater antiviral activity and better distribution into lymphoid tissues allows for reduced dosing with lower incidence of kidney and bone toxicity
- 2 doses – 25mg daily without interacting antiretrovirals (ARVs) or 10mg daily if used in combination with ritonavir or cobicistat

Gilead Press Release

TAF COMBOS

- November 2014 –
- NDA submitted to FDA for new TAF version of Stribild®
- FDA approved Genvoya® 11/5/2015
- April 2015 –
- NDA submitted to FDA for new TAF version of Truvada®
- July 2015 –
- NDA submitted to FDA for new TAF version of Complera®
- Anticipated 2016 –
- Combination of TAF, emtricitabine, darunavir, cobicistat

GENVOYA



- Genvoya® 4 drug single tablet complete HIV regimen consisting of a combination of:
 - Elvitegravir – HIV-1 integrase strand transfer inhibitor (INSTI)
 - Cobicistat – CYP3A inhibitor with no HIV activity
 - Emtricitabine – HIV-1 nucleoside analog reverse transcriptase inhibitor (NRTI)
 - **Tenofovir alafenamide (TAF)** – HIV-1 nucleotide analog reverse transcriptase inhibitor (NRTI)
- ~~treatment of HIV-1 infection in adults and pediatric patients 12 years of age and older with renal function CrCL ≥ 30 mL/min~~

Genvoya® Package Insert Gilead 11/2015

RENAL EFFECTS

- No cases of Fanconi syndrome or Proximal Renal Tubulopathy (PRT) in clinical trials of Genvoya®
- Clinicians are encouraged to assess CrCL, urine glucose, and urine protein in all HIV patients and serum phosphorus in HIV patients with CKD before initiating Genvoya® and monitor periodically during therapy

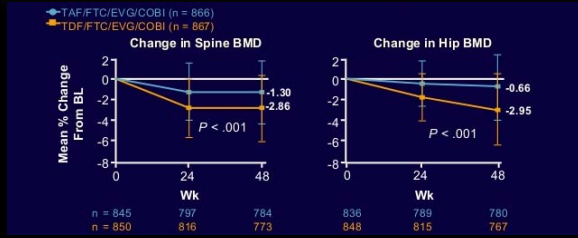
Genvoya® Package Insert Gilead 11/2015

BMD EFFECTS

- HIV treatment naïve patients
- Evaluated bone mineral density (BMD) from baseline to Week 48 by DEXA to compare the bone safety of TAF to that of tenofovir in Genvoya® vs Stribild®
- Mean BMD declines with Genvoya® vs Stribild®
 - lumbar spine -1.30% vs -2.86%
 - total hip -0.66% vs -2.95%
- Total BMD Decreases
 - $\geq 5\%$ lumbar spine 10% vs 22%
 - $\geq 7\%$ femoral neck ~~7% vs 10%~~
- Fractures low incidence 0.8% vs 1.4%

Genvoya® Package Insert Gilead 11/2015

BMD EFFECTS



Sax, P et al. CROI 2015 Abstract 143

BMD EFFECTS

- HIV treatment experienced patients
- Evaluated BMD from baseline to Week 48 by DEXA to compare the bone safety of continuing a tenofovir based ART regimen or switching to TAF in Genvoya®
- Mean BMD increases with TAF in Genvoya® vs tenofovir
 - lumbar spine 1.86% vs -0.11%
 - total hip 1.95% vs -0.14%
- Total BMD Decreases
 - ≥5% lumbar spine 1% vs 6%
 - ≥7% femoral neck 1% vs 4%
- Fractures low incidence 1% vs 0.4%

Genvoya® Package Insert Gilead 11/2015

ASSESSMENT

- Questions:
- What are some key patient counseling points for patients changing from tenofovir to TAF regimens?
- When patients change to TAF do they no longer need any renal monitoring labs?

PATIENT COUNSELING

- Key points to patient counseling for patients changing from tenofovir to TAF regimens
 - less impact on kidneys
 - less impact on bones
 - important to keep follow up appointments with your doctor and get labs because all HIV medications need to be monitored for safety and efficacy

CONCLUSION

- HIV is a treatable chronic medical condition
- Tenofovir is a central component of the majority of HIV medication prevention and treatment regimens
- Concerns over long term bone safety and nephrotoxicity led Gilead to develop TAF
- Anticipate 4 TAF containing HIV combination products to be FDA approved and available to HIV patients within the next year
