2018 HIV Treatment and Prevention Updates

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Disclosure

- Nothing to disclose at this time

Objectives

- View the latest HIV Stats
- Discuss new the newest antivirals to the market
- Discuss the new HIV/AIDs treatment updates
- Discuss the new HIV prevention updates
- Discuss pipeline medications for HIV/AIDs

HIV Stats

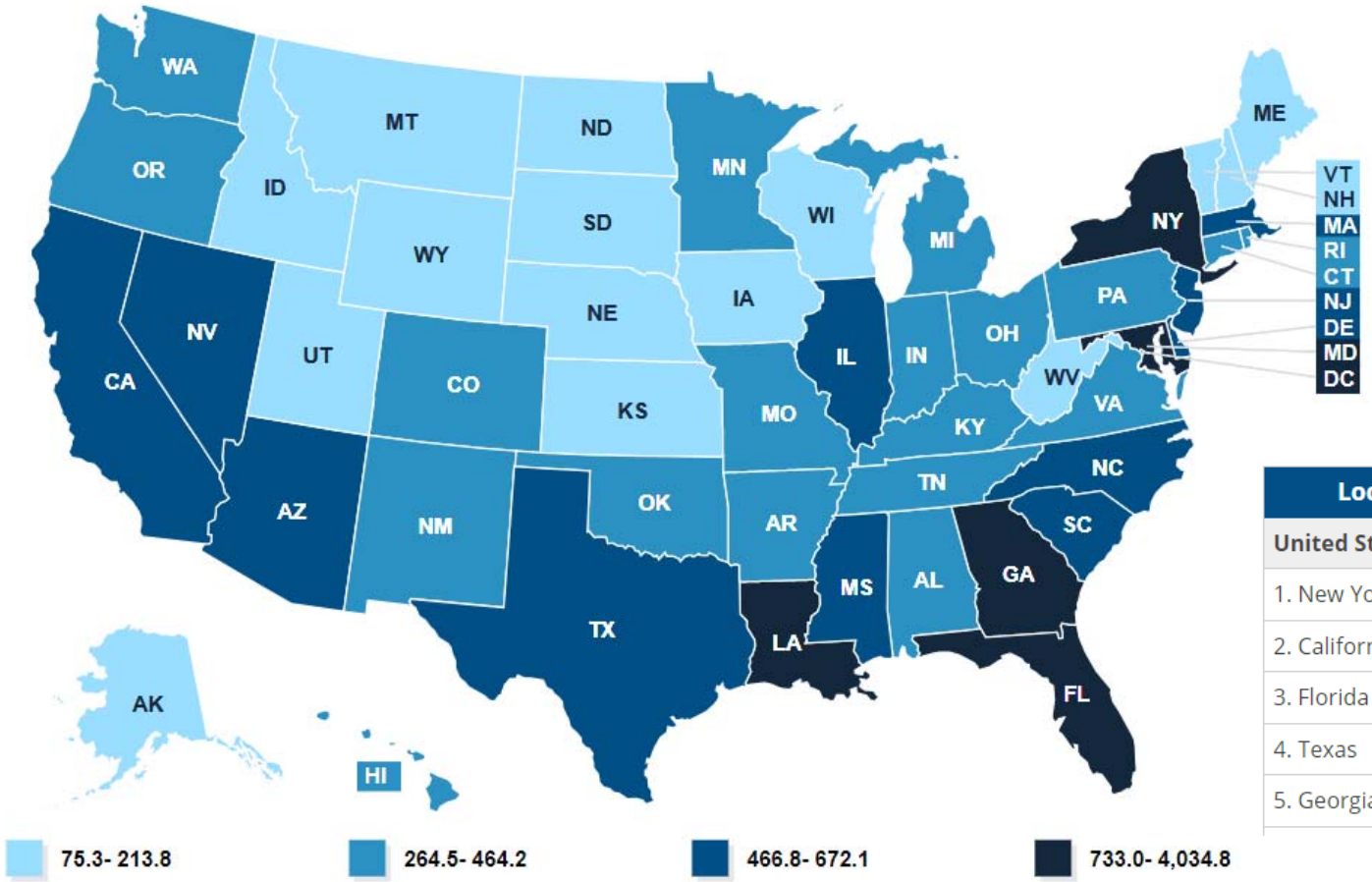
Where are we today with the numbers

United States HIV Diagnosis, 2016

- Newly diagnosed: 39,782
  - Males (13 years or older): 32,131
  - Females (13 years or older): 7,529
  - Children (<13 years): 122
- 5 Top States for newly diagnosed cases:
  - California: 4,972
  - Florida: 4,957
  - Texas: 4,472
  - New York: 2,877
  - Georgia: 2,716

CDC: https://www.cdc.gov/hiv/statistics/overview/index.html

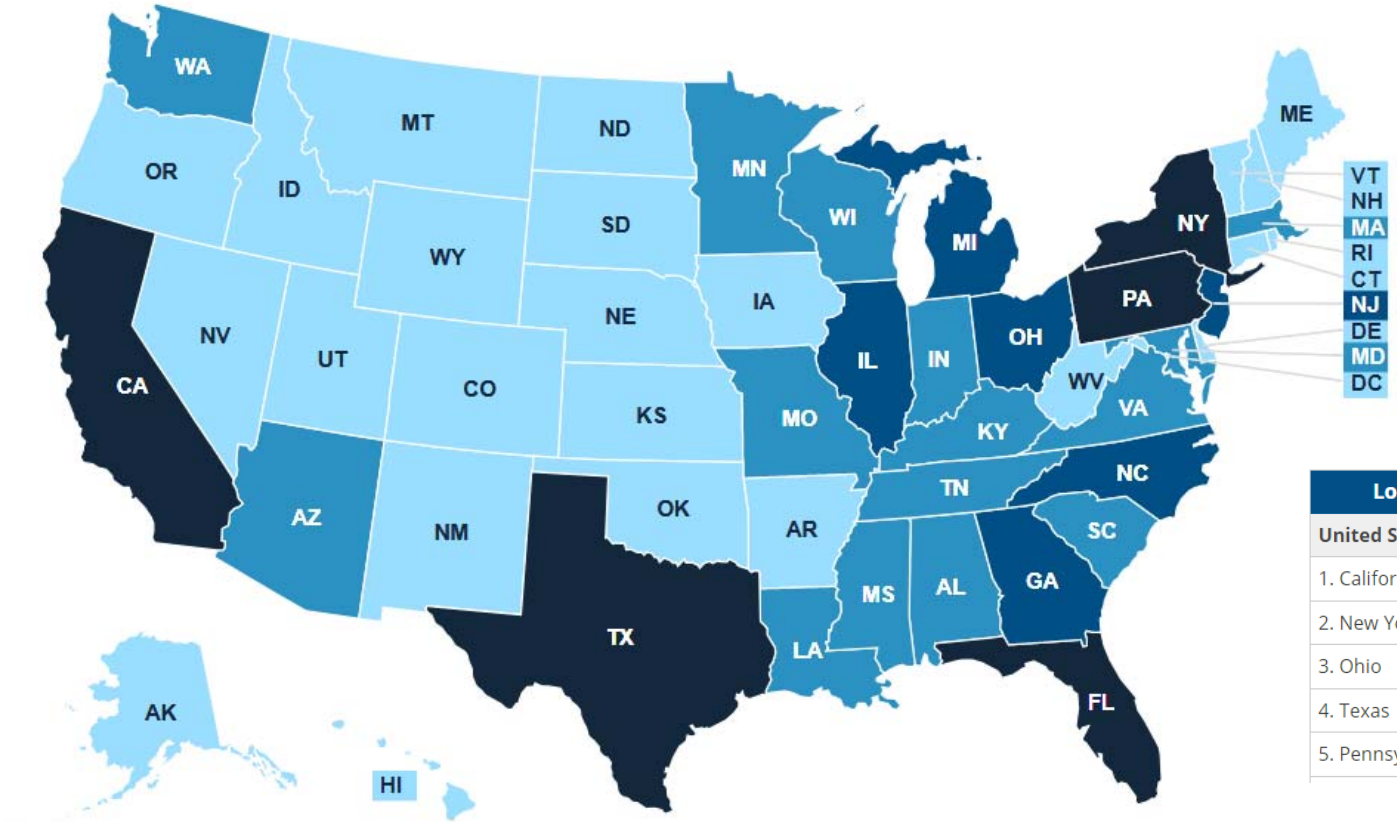
State Health Facts: # Adults and Adolescents Living with HIV, 2015



Location	Total
United States [1]	971,524
1. New York	128,681
2. California	122,079
3. Florida	106,585
4. Texas	81,873
5. Georgia	49,463

Henry J Kaiser Family Foundation: https://www.kff.org/

of Retail RX by Medicaid, 2017



Location	Medicaid
United States	643,405,963
1. California	73,787,097
2. New York	66,602,399
3. Ohio	40,292,739
4. Texas	32,295,285
5. Pennsylvania	31,866,100

5,138,778- 51,301,839 | 51,889,427- 106,646,670 | 109,615,113- 171,487,283 | 182,320,267- 358,944,105

Henry J Kaiser Family Foundation: https://www.kff.org/

Newer Antivirals

Newer ART

- New Products/Formulations:
  - Raltegravir HD (2017)
  - **Ibalizumab** (03/2018)
- New Combination products:
  - **Bictegravir**, emtricitabine and tenofovir alafenamide (02/2018)
  - Darunavir, cobicistat, emtricitabine and tenofovir alafenamide (07/2018)
  - Dolutegravir and rilprivirine (11/2017)
  - Efavirenz, lamivudine and tenofovir disoproxil fumarate (03/2018)
  - Efavirenz, lamivudine and tenofovir disoproxil fumarate – LO (02/2018)
  - Lamivudine and tenofovir disoproxil fumarate (02/2018)

Raltegravir HD, 2017

- Drug Class: Integrase Inhibitor
- **H**igh **D**ose formulation; enteric coated; no food restrictions
- Raltegravir one 400mg tablet BID vs HD 2-600mg tabs QD
- Must be at least 40kg
- Tough competition
- AWP = $1800/month

Ibalizumab, 2017

- Drug class: Post-Attachment Inhibitor (monoclonal antibody); **orphan drug** designation
- Mechanism of Action: Attached to the CD4 cell to prevent HIV entry = no viral replication
- Who is a candidate:
  - **Heavily treatment experienced with multi-drug resistance**
  - HIV is not well controlled
- Administration: used in combination of other HIV medications
  - Starting dose: 2000mg IV infusion over 15-30 minutes then every two weeks the maintenance dose of 800mg **IV infusion by a trained medical professional**
- Side Effects: diarrhea, nausea, dizziness and rash
- AWP = not yet established
- Enrollment form to be faxed to THERA

Trogarzo: http://www.trogarzo.com/

Bictegravir/emtricitabine/ tenofovir alafenamide (02/2018)

- Drug Class: Single Tablet Regimen (InSTI + 2-NRTIs)
- Administration: once daily without regard to food
- Not approved for pregnancy or breast feeding
- Contradictions: CrCL <30 mL/min, severe liver issues
- Side Effects: nausea and vomiting (severe: lactic acidosis, liver complications)
- DDI: avoid rifampin, dofetilide, St John's wort; monitor metformin; 2 hours separation for laxatives or antacids, oral iron and calcium supplements
- AWP = $3534.78/month

Biktarvyhttps://www.biktarvy.com/

Darunavir/cobicistat/emtricitabine/tenofovir alafenamide (07/2018)

- First protease inhibitor single tablet regimen
- Not yet on the market
- Benefit: PIs high genetic barrier to resistance
- Sulfa component
- Administration: Once daily with food
- Side effects: nose/throat inflammation, upper respiratory infection, diarrhea
- DDI: many (cobicistat inhibits liver enzymes)
- AWP = unknown yet

Dolutegravir and Rilprivirine (11/2017)

- Drug Class: Single Tablet Regimen (InSTI + NNRTI)
- Administration: Once daily with a meal
- Requirements: must be virologically suppressed and no treatment failures/resistance mutations to product
- Side Effects: diarrhea and headache; neuropsychiatric effects
- DDI: dofetilide, carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifapentine, proton pump inhibitors, St. John's wort, dexamethasone
- AWP = $3094.80/month

Juluca: https://us.juluca.com/

2018 HIV Treatment Updates

IAS Conference 2018

HIV Information/Guidelines

- DHHS: Department of Health & Human Services
  - https://aidsinfo.nih.gov/guidelines
- IAS-USA: International Antiviral Society
  - https://www.iasusa.org/guidelines
- WHO: Worlds Health Organization
  - http://www.who.int/hiv/pub/guidelines/en/
- Infectious Diseases Society of America
  - http://www.idsociety.org/FDA_20140502.aspx

DHHS Guidelines, March 2018

- Initial Start: ART recommended for all, regardless of CD4
- 3 Treatment should include **3 ACTIVE medications** from at least **2 different classes**
  - No resistance
  - Booster do not count
- Generally consists of **two Nucleos(t)ide Reverse Transcriptase Inhibitor (NRTIs)** with a third active agent from 1 of the 3 drug classes:
  - **Integrase Inhibitors (InSTIs)**
  - **Non-Nucleos(t)ide Reverse Transcriptase Inhibitors (NNRTIs)**
  - **Protease Inhibitors (PI)** with booster

DHHS: https://aidsinfo.nih.gov/guidelines/brief-html/1/adult-and-adolescent-arv/11/what-to-start

DHHS Preferred, Initial

- Dolutegravir/abacavir/lamivudine—**only** for patients who are HLA-B*5701-negative
- Dolutegravir plus tenofovir/emtricitabine
- Elvitegravir/cobicistat/tenofovir/emtricitabine
- Raltegravir plus tenofovir/emtricitabine (**TDF or TAF**)

DHHS: https://aidsinfo.nih.gov/guidelines/brief-html/1/adult-and-adolescent-arv/11/what-to-start

HIV 2018 Updates IAS-USA

Clinical Review & Education

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

IAS Panel

- 16 volunteer experts in HIV research and patient care
- Reviewed data published or presented from September 2016 through June 2018
- Rated on strength of recommendation and quality of evidence (see table 1 from JAMA for scale)
- Last IAS-USA guidelines dated back from 2016

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

2018 IAS-USA Antiretroviral Guidelines: Key Updates

- Recommend initial regimens focus on unboosted (InSTI) regimens
- Encourage rapid initiation of ART, including "same day" initiation
- Dolutegravir: neural tube defects
- Recommend discontinuation of routine CD4+ counts once a patient has a sustained undetectable HIV RNA for a year and has a CD4+ count $\geq$ 250 cells/uL
- Expand alternatives for preexposure prophylaxis for MSM who are uninfected with HIV but remain at risk; the episode-based "2-1-1" approach

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

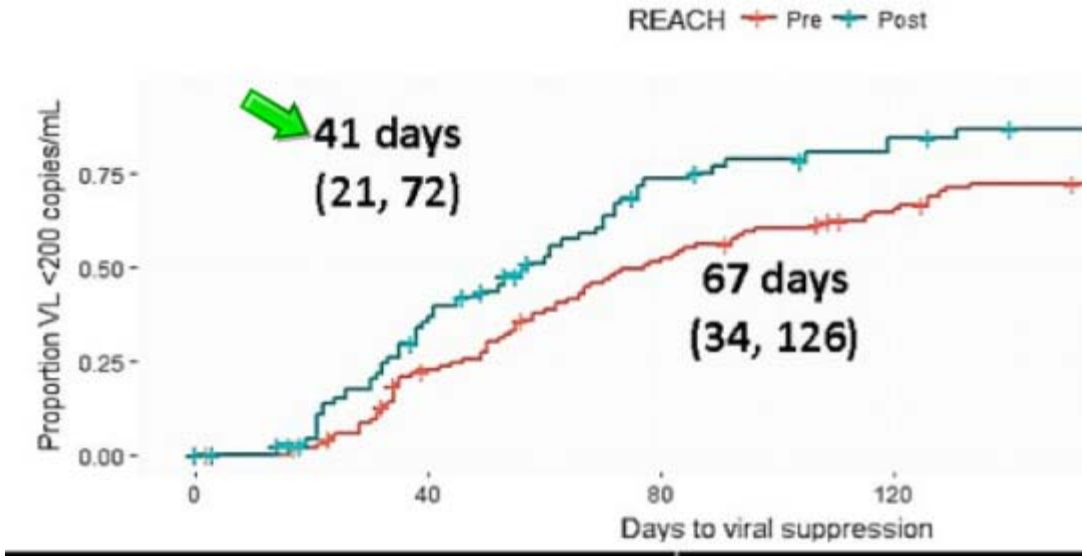
Recommendations for the Initiation of Antiretrovirals (ART)

- When to Start
  - Immediately after diagnosis
    - Rapid ART Start (same day as diagnosis) vs
    - 14 days after diagnosis
- Lab samples: HIV-1 RNA level; CD4 cell count; HIV genotype for NRTI, NNRTI, and PI; HLA-B*5701 testing; laboratory tests to exclude active viral hepatitis; and chemistries should be drawn before beginning ART
- **Treatment may be started before results are available**

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

Rapid Entry Program Grady in Atlanta, GA

- Grady reduced barriers, with goal to begin ART within 72 hours



Saag, Benson, Gandhi, et al, *JAMA*, 2018
Colasanti, et al, Open Forum Infectious Disease, 2018

Recommended Rapid ART Regimens

- InSTI + 2 nRTIs
  - Bictegravir/TAF/emtricitabine
  - Dolutegravir/abacavir/lamivudine
  - Dolutegravir plus TAF/emtricitabine
- AVOID for Rapid:
  - NNRTIs (possible transmitted resistance)
  - abacavir (without HLA-B*5701 results)

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

Recommended Initial: If InSTI Not Available

- Darunavir/cobicistat plus 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 copies/mL and CD4 cell count is >200/μL)

*Fixed-dose D/c/TAF/FTC approved July 2018

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

Treatment Overview

- There are many treatment options for initial therapy that are equally efficacious.
- Selection is guided by toxicity, pill burden, dosing frequency, drug-drug interaction potential, resistance results, comorbid condition and cost.

NOT RECOMMENDED:

★ Monotherapy

★ Dual or triple-NRTI regimens alone

Dolutegravir and Pregnancy

- DHHS guidelines updated to reflect findings
- Birth Outcomes Study in Botswana in 2014
- Goal: Evaluate birth outcome by HIV status and ARV regimen and to assess whether increased risk of NTD among infants exposed to EFV
- Midwifes trained to do exams and alert research assistant
- In 2016, Botswana switched from TDF/FTC/EFV to TDF/FTC/DTG for all adults

IAS Webinar for 2018 HIV updates: https://www.iasusa.org/

Dolutegravir and Pregnancy, continued

- Results:
  - ~89,000 births
    - 426 patients on DTG from conception
    - 11,300 patients on non-DTG from conception
  - 86 neural tube defects identified total
  - **DTG at conception: 4/426 (0.94%)**
  - Non of the women appeared to be on folate supplementation
- Conclusion: more neural tube defects were found than expected

2018 HIV Prevention Updates

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3 ways ART used as Prevention

- Treatment as prevention (TasP)
- Preexposure prophylaxis (PrEP)
- Postexposure prophylaxis (PEP)

PrEP Updates

- Still only one medication: TDF/emtricitabine
- Transgender role: consider E2 interaction with TDF
- Now FDA approved for teens: 77lbs or greater
- “2-1-1” PrEP regimen not FDA approved by endorsed by many organizations
- TAF is not an approved PrEP regimen

The Future: HIV Pipeline Medications

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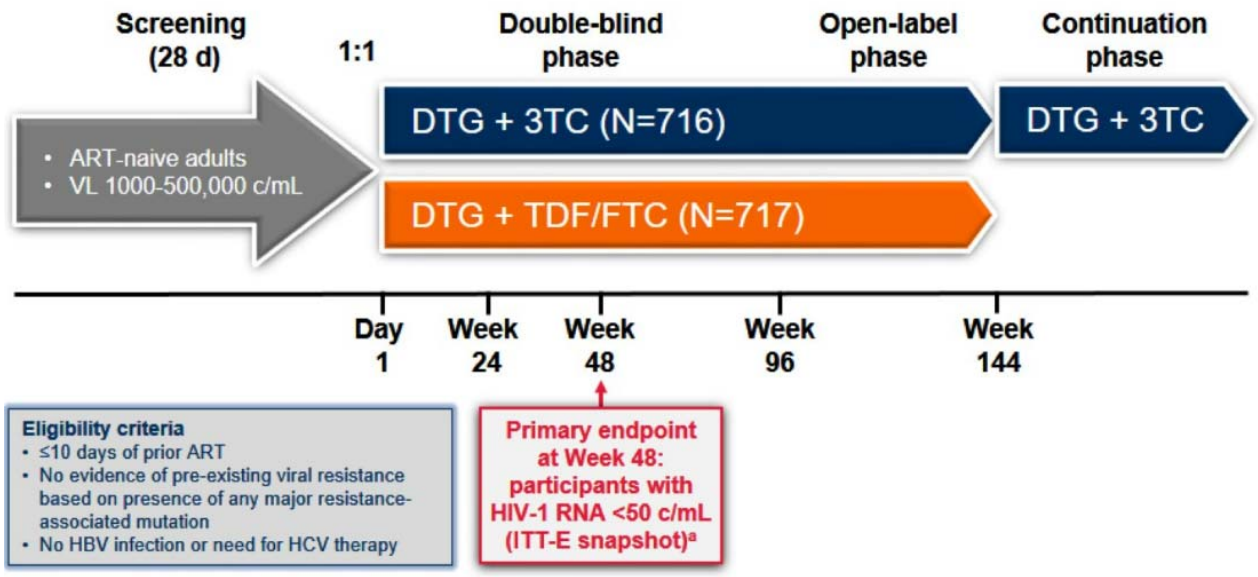
Pipeline Therapies

- Entry Inhibitor: Albuvirtide, Once weekly injections
- NNRTIs: doravirine (mono tablet and STR)
- Dolutegravir/3TC (GEMINI study)
- Long Acting: cabotegravir
- Monoclonal Antibody:
  - PRO 140 as once weekly injection
  - UB-421 infusion
- Latency Reversing Agents

The BodyPro: http://www.thebodypro.com and i-base: http://i-base.info/htb/34488

GEMINI-1 and -2 Study

Randomized, double-blind, parallel-group, multicenter, non-inferiority (Δ10%) studies



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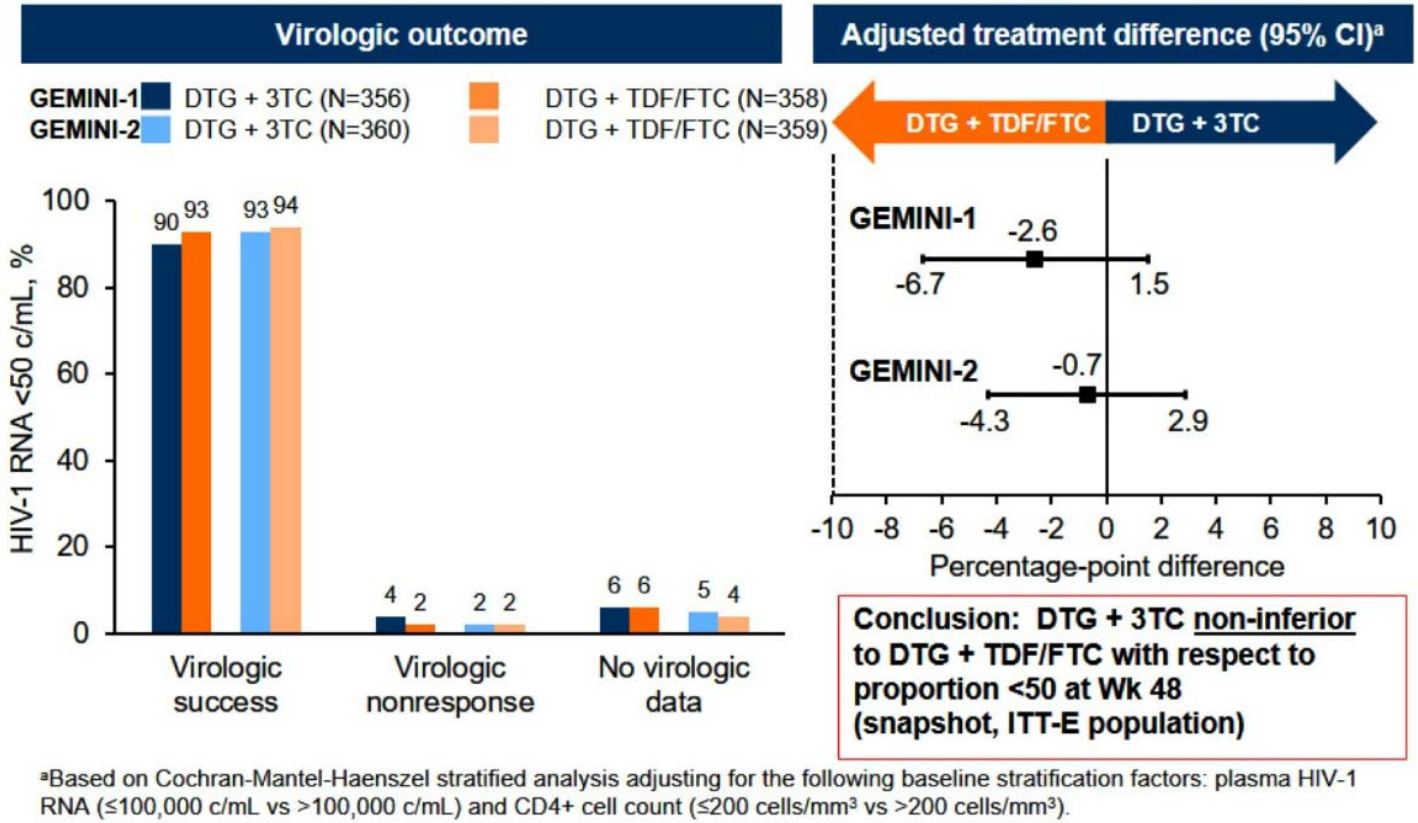
Gemini-1 and -2 Study



[a]Based on Cochran-Mantel-Haenszel stratified analysis adjusting for the following baseline stratification factors: plasma HIV-1 RNA (≤100,000 c/mL vs >100,000 c/mL) and CD4+ cell count (≤200 cells/mm³ vs >200 cells/mm³).

IAS Webinar for 2018 HIV updates: https://www.iasusa.org/

Cure Status?

- Berlin Patient: Timothy Brown
  - I am the Berlin Patient: A personal Reflection
  - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4287108/
  - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4576177/
- At least 6 more HIV men attempted Berlin Treatment but it has failed.
  - http://www.natap.org/2015/CROI/croi_98.htm

Conclusions

- HIV treatment options are increasing with many new drug classes in the near pipeline
- Goal: 90/90/90 by 2020 worldwide for HIV/AIDs
  - 90% of people will be diagnosed
  - 90% of people with HIV will be on medications
  - 90% of people with HIV will be virally surpressed
- Expect frequent updates to the guidelines
- Thank you for your time!