2020 Ryan White HIV/AIDS Program CLINICAL CONFERENCE

Updates from Recent HIV Research Conferences: CROI 2020 and AIDS 2020

Roy M. Gulick, MD, MPH
Rochelle Belfer Professor in Medicine
Weill Cornell Medicine
New York, New York

Financial Relationships With Commercial Entities

Dr Gulick has no relevant financial affiliations to disclose. (Updated 08/05/20)

Slide 2 of 36

Learning Objectives

After attending this presentation, learners will be able to:

- Identify new trends in HIV epidemiology
- Apply the latest data in HIV treatment to patient care
- Discuss the latest data in HIV prevention strategies

Slide 3 of 36

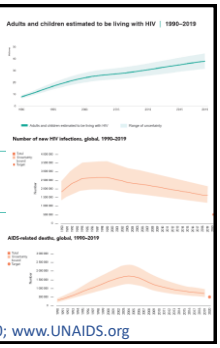
Meeting Highlights

- Epidemiology
- Antiretroviral therapy
  - What to start?
  - Resistance
  - Weight gain
  - Pregnancy
  - New drugs
- Prevention
- Cure

Epidemiology

Global summary of the AIDS epidemic | 2019

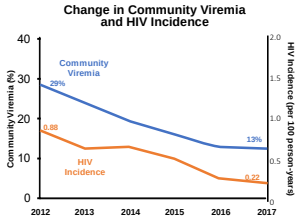
Number of people living with HIV	Total	38.0 million	[31.6 million–44.5 million]
	Adults	36.2 million	[30.2 million–42.5 million]
	Women (15+ years)	19.2 million	[16.4 million–22.2 million]
	Children (<15 years)	1.8 million	[1.3 million–2.2 million]
People newly infected with HIV in 2019	Total	1.7 million	[1.2 million–2.2 million]
	Adults	1.5 million	[1.1 million–2.0 million]
	Children (<15 years)	150 000	[94 000–240 000]
AIDS-related deaths in 2019	Total	690 000	[500 000–970 000]
	Adults	600 000	[430 000–840 000]
	Children (<15 years)	95 000	[61 000–150 000]



UNAIDS data 2020; www.UNAIDS.org

Community Viremia (>200 c/ml) and HIV Incidence in Australia

- Longitudinal cohort study (2012-2017)
  - Gay/bisexual men with (n=14,839) and w/o (n=101,143) HIV
  - Data from sentinel surveillance system of 34 sexual health clinics, 25 general practices, 5 community HIV-testing sites, and 3 hospitals (New South Wales and Victoria – 60% of Australians)
- From 2012 to 2017
  - HIV viremia ↓
    - With HIV: ↓ 17% to 4% (*P*<0.001)
    - Undiagnosed HIV: ↓ 11% to 9% (*P*=0.5)
    - Community: ↓ 29% to 13% (*P*<0.001)
  - HIV incidence ↓ 0.88 to 0.22 per 100 person-years (*P*<0.001)
- Conclusion: ↓ community viremia was strongly associated with ↓ HIV incidence (*P*<0.001), including before PrEP



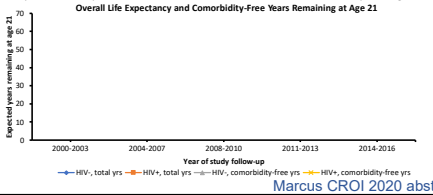
Callander CROI 2020 abstract #48

Kaiser: Life Expectancy of People with/without HIV

Cohort of adults with HIV in care 2000-2016 (N=39,000)
Matched 1:10 with uninfected (N=387,767)
Study population:
Avg 41 yo, Asian 5%/Black 25%/Latinx 24%/white 45%, MSM 70%, HS 20%, IDU 8%

Results: Narrowing of the survival gap – now 9 years shorter with HIV vs no HIV

- Gap = 0 years if ART initiated before CD4 < 500
- No improvement in years without comorbidities (cancer, DM, CV, liver, kidney, or lung disease)



Marcus CROI 2020 abstract #151

Veterans Administration Cohort Study (VACS): COVID-19

- Open cohort of all veterans with HIV and matched 1:2 for age, race/ethnicity, site with veterans without HIV

	PLWH		HIV-uninfected			
	N	%	N	%	OR/HR	95% CI
Alive in 2020	30,948		76,618			
Tested for COVID-19	1486	4.8%	2735	3.6%	**1.39**	**(1.30, 1.49)**
COVID-19 +	189	0.6%	380	0.5%	1.39	(1.16, 1.66)
Outcomes						
ICU admission	32	16.0%	72	18.9%	0.94	(0.51, 1.73)
intubation	15	7.9%	35	9.2%	0.99	(0.65, 1.49)
death	18	9.5%	47	12.4%	0.96	(0.56, 1.67)

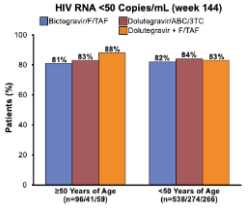
- Conclusions: PLWH higher rate of testing, but **no differences** in infection or complication rates vs. uninfected

Park IAS 2020 #LBPEC23

ART: What to Start?

Pooled Analysis of Studies 1489 and 1490: BIC vs. DTG in Persons ≥50 Years of Age

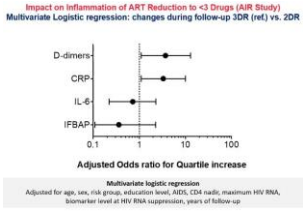
- Two phase 3 studies in treatment-naïve patients
- TAF/FTC/bictegravir versus dolutegravir-based ART (with ABC/3TC or F/TAF)
- HIV RNA <50 copies/mL at week 144
- Results:
  - Comparable safety and efficacy in ≥50 years of age, overall study population, and <50 years of age
  - No resistance in any treatment group



Mills CROI 2020 Abstract #477

Inflammation: 2- vs. 3-drug ART

- Retrospective COIRS cohort study
- N=8,415 otherwise healthy PLWH, suppressed on ART
  - 7,665 on 3-drug ART
  - 424 changed to 2-drug ART
  - 327 changed to 1-drug ART
- No difference in endpoints of death or end organ disease
- Biomarkers in 90 (3-drug ART), 60 (2-drug ART), 30 (1-drug ART)

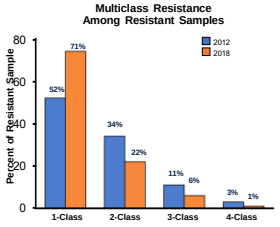


Serrano-Villar IAS 2020 #OAB0303

ART: Resistance

Trends in HIV Drug Resistance in the United States (2012-2018)

- De-identified samples submitted for routine HIV resistance testing (n=84,611; 2012-2018)
  - Analysis restricted to samples demonstrating substantial genotypic resistance to ≥1 ART class
  - Samples with resistance: 33%
- Change in resistant samples from 2012 to 2018
  - Resistance to NNRTIs was common/consistent (76% → 73%)
  - Resistance decreased over time to:
    - NRTIs (55% → 41%)
    - PIs (15% → 8%)
    - INSTIs (20% to 17%)
    - multiclasses
    - 4-class resistance was rare (1%)
- Trends correspond with availability of improved and more convenient ART options



Henegar CROI 2020 abstract 521

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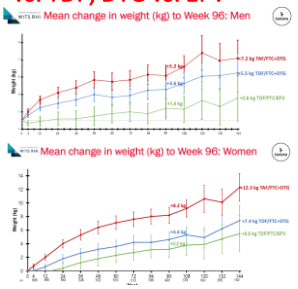
ART: Weight Gain

Advance Study: TAF vs. TDF; DTG vs. EFV

- South African PLWH, ART-naïve randomized to:
  - TDF/FTC/EFV
  - TDF/FTC + DTG
  - TAF/FTC + DTG (N=~350 per arm)
- Results:
  - VL <50 c/ml (ITT, wk 96): 74% (EFV), 78% (TDF/DTG), 79% (TAF/DTG)
  - More RTI resistance in EFV arm
  - Weight gain
  - Hip osteopenia: 16/351(5%)TAF vs. 58/608(10%)TDF



Sokhela IAS 2020 #OAXLB0104

What About Stopping TAF?: TANGO Study

- Pts on 3-drug regimen with TAF at suppressed VL randomized 1:1 to continue or change to 2 drugs: DTG/3TC (N=686)
  - Only 8% women
- Results:
- 2 drugs non-inferior to 3 drugs in virologic suppression

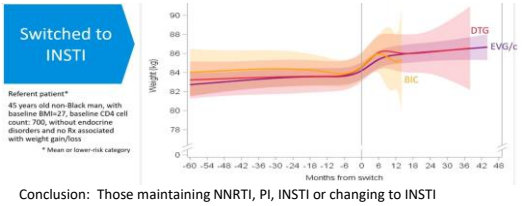
Weight parameter	DTG/3TC (N=343)	TAF-based regimen (N=343)
Adjusted[b] change from baseline, mean (SE), kg	0.81 (0.23)	0.76 (0.22)
Prior TAF duration <1 y[c]	1.45 (0.46)	1.35 (0.47)
Prior TAF duration ≥1 y[d]	0.60 (0.26)	0.60 (0.25)
Increased from baseline, n (%)		
≥10%	11 (3)	13 (4)

- Changing to DTG/3TC not associated with weight loss by 48 weeks

Van Wyk CID (epub 1/6/20)
van Wyk IAS 2020 #0606

OPERA Cohort – U.S.

- Analyzed 6,919 pts on ART with VS who ΔTDF to TAF and maintained 3rd drug or changed to INSTI

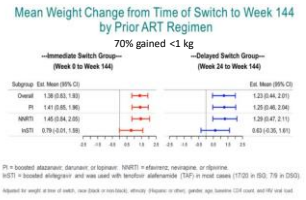


Conclusion: Those maintaining NNRTI, PI, INSTI or changing to INSTI had similar weight gain with Δ TDF to TAF

Mallon IAS 2020 #OAB0604

Change to DOR/3TC/TDF – Effect on Weight

- Change from PI-, NNRTI- or INSTI-based regimen to DOR/3TC/TDF (2:1; immediate vs. delayed) (N=656)
- Post-hoc analysis of weight trends
- Conclusion: Patients on TAF+INSTI at baseline did not lose weight by week 48 after switch to TDF+DOR

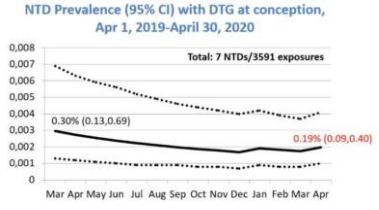


Kumar IAS 2020 #OAB0603

ART: Pregnancy

Tsepamo Update: DTG and Neural Tube Defect (NTD) Risk

Continued f/u of birth defects in Botswana (2014→4/20; ~70% of live births)



Non-DTG at conception: 0.11%

DTG during pregnancy 0.04%

HIV- women: 0.07%

- Conclusion: 1 excess neural tube defect/1000 treated during conception

Zash IAS 2020 #OAXLB0102

VESTED: IMPAACT 2010: ART in Pregnancy

Study population: ART-Naïve, pregnant WLHIV 14-28 weeks gestation in 9 countries (88% in Africa) (N=639)

Study rx: DTG+FTC/TAF vs DTG+FTC/TDF vs EFV/FTC/TDF

Results:

VL <200 at delivery: 97.5% (DTG) vs. 91.0% (EFV)

Risk difference 6.5% (2.0%, 10.7%) → DTG superior

Two babies born with HIV:

— TAF/FTC/DTG: maternal viral load 58K

— TDF/FTC/DTG: maternal viral load < 40

Pregnancy Adverse Outcomes (all, including preterm delivery and small for getstational age): 24% (TAF/DTG) vs. 33% (TDF/DTG and /EFV)

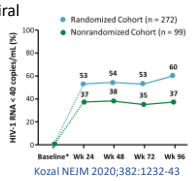
Chinula CROI 2020 abstract #130LB

ART: New Drugs

2020 Mar 26;382(13):1232-1243.

Fostemsavir (FTR)

- Fostemsavir (FTR): Small-molecule that binds to gp120 and prevents attachment – new antiretroviral class: CD4 attachment inhibitor
- BRIGHTE (Phase 3): heavily rx-experienced PLWH
  - n=272 with 1-2 remaining ART classes randomized to FTR 600 mg bid or placebo
  - N=99 with no remaining ART classes not randomized; all received FTR
- U.S. FDA approved for adults living with HIV who have tried multiple HIV meds and whose HIV infection cannot be successfully treated with other therapies because of resistance, intolerance or safety considerations.

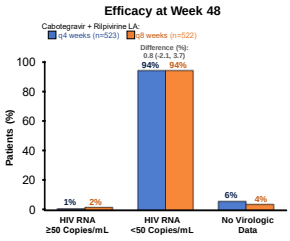


Kozal NEJM 2020;382:1232-43

Lataillade IAS 2019 #MOAB0102

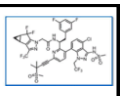
ATLAS-2M Study: CAB + RPV LA Q4 Versus Q8 Weeks

- Phase 3b, open-label non-inferiority (Δ4%) study (N=1045)
- Study pop: ATLAS pts – on SOC ART or CAB+RPV LA with VL <50
- Study rx: (po lead in of CAB+RPV X 4 wks if on SOC ART)
  - CAB 400 + RPV 600 LA q4 wks or CAB 600 + RPV 600 LA q8 wks
- Results:
  - Safety: ISR 98% were grade 1-2, median duration 3 days
- Conclusion: q8 weeks was non-inferior to q4 weeks

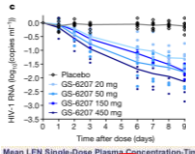


Overton CROI 2020 Abstract 34

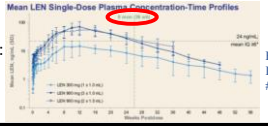
Capsid Inhibitor: Lenacapavir (LEN, GS-6207)



- Potent antiretroviral activity: EC_{50} 140 pM in PBMC
- Active across all tested subtypes
- Resistant variants have low fitness
- ↓ clearance and solubility → very long ½ life: 30-43 days
- Oral and SC formulations
- Phase 1 in HIV- and HIV+ pts
  - Max VL ↓ 2.2 log cps/ml at day 10
- New sustained-delivery formulation:
  - Phase 1 in 30 HIV- pts
  - 3 SC doses (10/group)

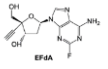


Link Nature (epub 7/1/20)



Begley IAS 2020 #PEB0265

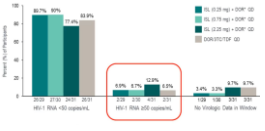
Islatravir (ISL): NRTTI



- EFdA – adenosine analogue
- Active against NRTI-resistant virus
- Half-life = 50-60 hours in plasma
- Oral and parenteral formulations

- Phase 2b study of ISL+DOR+3TC vs. DOR/3TC/TDF; ISL: 3TC d/c at 24 wks
  - Treatment-naïve (N=120)
- Results
  - At week 48 viral suppression similar
  - VL too low for resistance testing
  - Adverse effects similar; mild HA more common for ISL (11%), transient
- Phase 3 planned: rx-naïve, switch, rx-experienced (ISL dose 0.75 mg)

48 weeks: FDA Snapshot

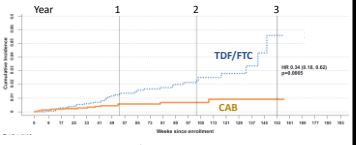


Molina J-M IAS 2019 #WEAB0402LB
Orkin IAS 2020 #OAB0302
DeJesus IAS 2020 #OAB0304

Prevention

HPTN 083: PrEP with IM CAB vs. TDF/FTC

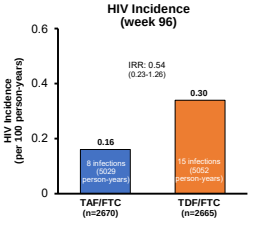
- Phase 2b/3 randomized, double-blinded HIV PrEP international study
- Study pop: High-risk adult MSM/TGW (N=4570)
  - 67% <30 yo; 12% TGW; 50% Black in U.S.
- Study reg: CAB oral (5 wks)→IM q2 mos vs. TDF/FTC po daily
- DSMB stopped study early!
- Results:
  - New HIV infections:
    - 13 (CAB) vs. 39 (TDF/FTC)
  - HIV incidence rates (/100 pt yrs):
    - 0.41 (CAB) vs. 1.22 (TDF/FTC)
  - Safety:
    - ISR 81% (CAB) vs. 31% (placebo)
    - 2% of CAB participants d/c
- Conclusion: CAB non-inferior and superior!



Landovitz IAS 2020 #OAXLB0101

PrEP: DISCOVER: TAF/FTC vs TDF/FTC (96 weeks)

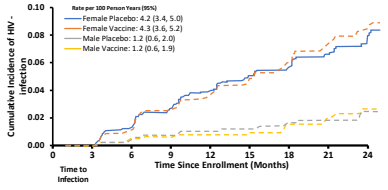
- Phase 3, double-blind randomized study of MSM and TGW at-high risk for HIV with eGFR ≥60 (N=5387)
- Study population:
  - Average age: 34 years
  - Asian 5%/Black 9%/white 84%; TGW: 2%
- Results:
  - PrEP with TAF/FTC was non-inferior to TDF/FTC for new HIV infections at both week 48 and 96
  - Safety: D/C for AE: 1% (TAF) vs. 2% (TDF)
    - Bone/renal markers improved with TAF
  - Weight change:
    - TAF: +1.0 kg (wk 48) and +1.7 kg (wk 96)
    - TDF: 0 kg (wk 48) and +0.5 kg (wk 96) P<0.001



Ogbuagu CROI 2020 abstract #92

HVTN 702: HIV Vaccine Study in South Africa

Phase 2b/3 study of HIV vaccine (ALVAC + gp120/MF59) (N=5400)
Start 10/16 → DSMB stopped study in 2/20



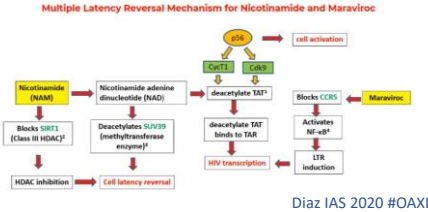
Gray CROI 2020 abstract #SS02

Cure

The Sao Paolo Patient

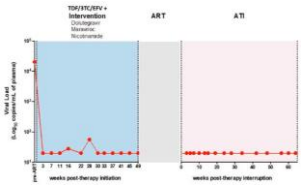
SPARC-7 Study of 30 pts on first-line ART, CD4 >350, VS X ≥2 yrs

Study Rx: add DTG+ maraviroc + nicotinamide to ART → change back to original ART regimen → ATI



Diaz IAS 2020 #OAXLB0105

1 patient post-ART Interruption:



- No detectable HIV RNA or DNA in blood
- PBMC co-culture negative for HIV
- HIV-EIA reverted to negative, but Western Blot positive
- No other study subjects in remission (n=29)

Diaz IAS 2020 #OAXLB0105

Thanks to:
IAS-USA
Jeff Lennox and Paul Sax for slides

Weill Cornell Medicine
rgulick@med.cornell.edu

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Question-and-Answer Session