HIV Treatment in 2018: What's New & How To Communicate Those Messages

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USCA
September 7, 2018

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The Association of Nurses in AIDS Care (ANAC)

ANAC is the leading professional HIV nursing association educating, connecting and advocating for nurses concerned about HIV and HIV-related care. Founded in 1987, ANAC represents nurses, nurse practitioners, and other health care providers worldwide. We promote a comprehensive, holistic and evidence-based approach to quality HIV care, and advocate for policies grounded in a human rights approach to health.

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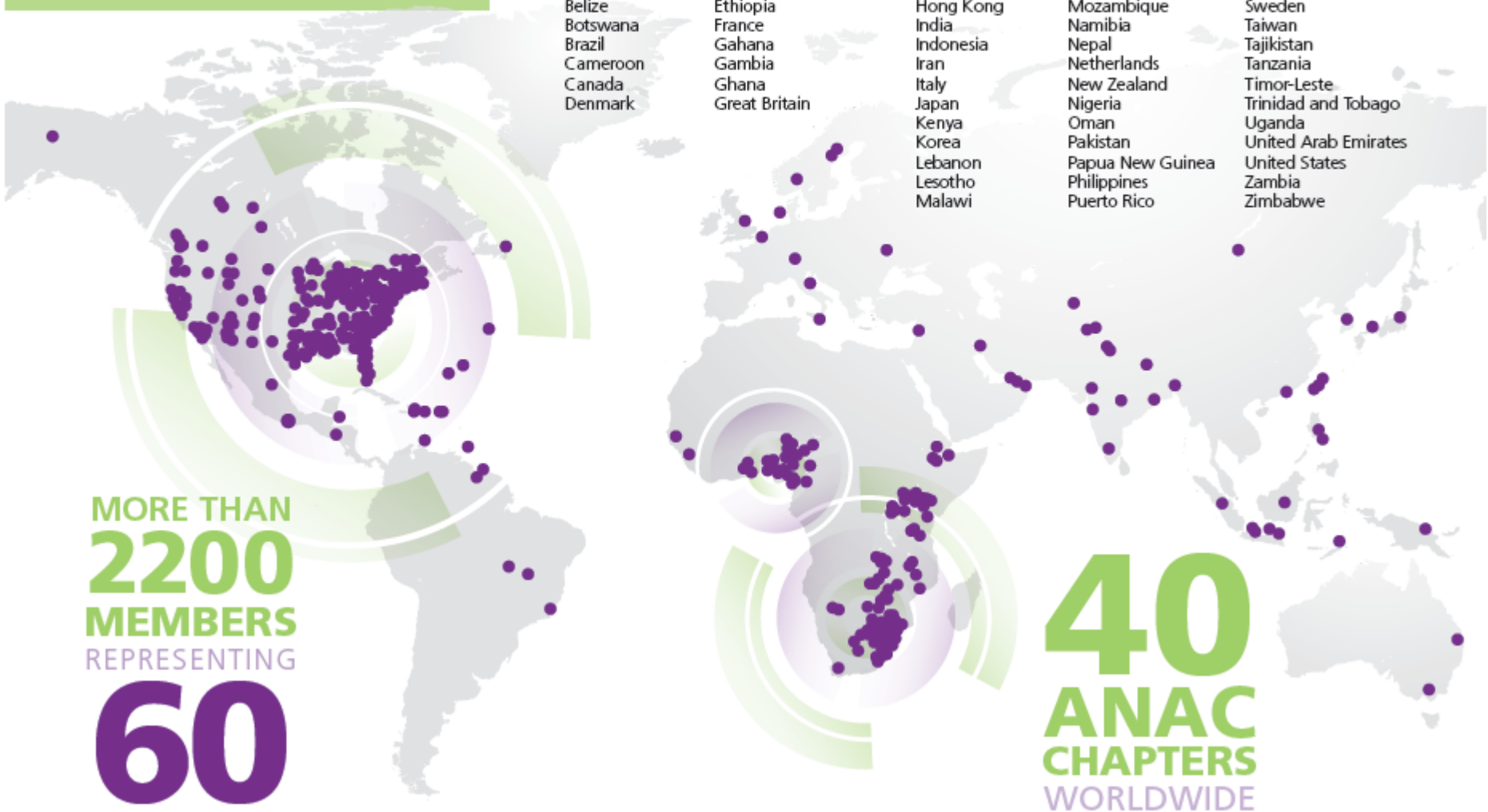

MORE THAN
2200
MEMBERS
REPRESENTING
60
COUNTRIES

40
ANAC
CHAPTERS
WORLDWIDE

Nurses in AIDS Care

Agenda
Resources & Opportunities

- Introductions
- HIV Treatment -Overview
- U=U
- Panel and Audience Q&A

Association of Nurses in AIDS Care www.nursesinaidscare.org

2018 Annual Conference

Denver November 8-10, 2018

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Objectives

1. Describe current recommendations for initiating HIV treatment.
2. List at least 2 treatment considerations in patients with underlying comorbidities.
3. Discuss recent advances in novel treatment options for HIV.

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Disclosures

- Jeffrey Kwong
  - Speakers Bureau, Gilead Sciences

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Case Challenge#1: LM

- 29 year old female referred following a new diagnosis of HIV infection.
- Seen earlier today at the Counseling & Testing Center at your health center where she was given her new HIV diagnosis.
- She has no significant past medical history and takes no medications.

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How would you approach this situation?

What are your priorities?

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Rapid Start

ART initiation recommended **as soon as possible** by DHHS and IAS-USA;

WHO recommends ART be offered **on day of diagnosis where feasible.**

1. DHHS Guidelines. May 2018. 2. Günthard HF, et al. JAMA. 2016;316:191-210.
3. WHO. July 2017. 4. Bacon O, et al. CROI 2018. Abstract O93.

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San Francisco's Rapid Start Program

Within 48 Hours:
if s/sx of Acute HIV or advanced disease
Within 5 days:
all other new HIV diagnosis

http://www.gettingtozerosf.org/rapid-committee/

Rapid Start: Outcomes

Outcome	2013	2014	2015	2016	% Change 2013- 2016
Diagnosed, n	399	329	295	265	--
Started ART, n (%)	311 (78)	276 (84)	244 (83)	215 (81)	--
Met RAPID definition, n (%)	23 (6)	45 (14)	50 (17)	80 (30)	--
In care within 1 yr, n (%)	372 (93)	318 (97)	282 (96)	258 (97)	--
Median time from diagnosis to care entry, d	8	7	7	5	-38
Median time from first care visit to ART initiation, d	27	17	6	1	-96
Median time from ART start to HIV-1 RNA < 200 c/mL, d	70	53	50	38	-46
Median time from diagnosis to HIV-1 RNA < 200 c/mL, d	134	92	77	61	-54

Time to first virologic suppression **decreased > 50% from 134 days to 61 days** and time from care linkage to ART start **decreased 96% from 27 days to 1 day**

Bacon O, et al. CROI 2018. Abstract O93.

Immediate ART: Considerations

ART initiation on day of HIV diagnosis **is resource-intensive**
…requiring systems in place to assure linkage to ongoing care.

US DHHS, 2018 available at www.aidsinfo.nih.gov

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Rapid Start Treatment Goals

- Goal of treatment is to suppress HIV RNA to below detectable levels (*AI*)

- Treatment **should not be withheld while awaiting the results of resistance testing;** adjustments may be made to the regimen once resistance results are available (*AIII*)

http://www.hivguidelines.org/clinical-guidelines/adults/diagnosis-and-management-of-acute-hiv-infection

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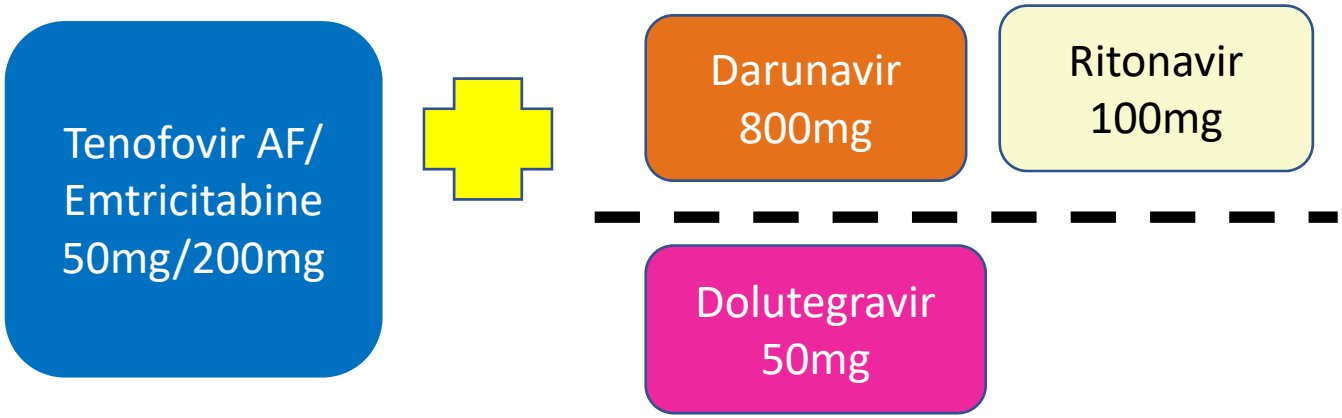
Choice of Treatment for Rapid Start



www.aidsinfo.nih.gov

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Early ART on Neurocognitive Function

- Sub-study from the START trial (early vs delayed ART)
- Assessed cognitive function in immediate(n=291) vs deferred (n=301)
- Followed for mean of 3.6 years

No differences in Neurocognitive Function In Immediate Vs Deferred

Wright et al. (2018). *AIDS* 32(8) 985-987.

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Case Challenge #2 JT

- 32 year old MSM diagnosed 6 months ago, but reluctant to start and was in and out of rehab.
- **Medical History**: depression, polysubstance abuse, syphilis, hepatitis C (treated in 2016), tobacco use, MRSA. Lowest HIV CD4 count = 525 cells/m^3
- **Social Hx**: Lives in a group home. Unemployed. GED

Presents today after completing 30 days of rehab

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Case Challenge #2

Laboratory Parameter	Results
HIV RNA	90,000 copies/ml
CD4+	569 cells/m^3
HCV RNA	< 15 IU/ml
Creatinine Clearance	102 ml/min
HIV Genotype	No Resistance
HLAB5701	Negative
RPR, GC/CT	Negative

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How would you address this situation?

Would you offer him treatment?

If yes – what?
If no – why not?

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Initial Antiretroviral Therapy

Regimen	US DHHS 2018	IAS-USA 2018
Bictegravir (BIC) + Emtricitabine (FTC)+Tenofovir AF (TAF)	X	X
Dolutegravir (DTG) + Emtricitabine (FTC)+Tenofovir AF(TAF)	X	X
Dolutegravir (DTG) +Lamivudine (3TC)+Abacavir (ABC)	X	X
Elvitegravir (EVG)+Cobicistat (COBI) + Emtrictabine (FTC)+Tenofovir AF (TAF) or TDF	X	
Raltegravir (RAL) +Emtrcitabine (FTC) + TAF or TDF	X	

US DHHS, 2018 available at www.aidsinfo.nih.gov; IAS-USA 2018 www.iasusa.org

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Bictegravir/Emtricitabine/Tenofovir AF: Key Information

Indications	▪ ART-naive pts ▪ Virologically suppressed
Key Drug-Drug interactions	▪ Contraindicated with dofetilide or rifampin ▪ Take 2 hrs **before** antacids containing Al/Mg or Ca ▪ Take with food if using supplements containing calcium or iron
Dose adjustments	▪ Not recommended in pts with CrCl < 30 mL/min

Prescibing Information, 2018 BIC/FTC/TAF.

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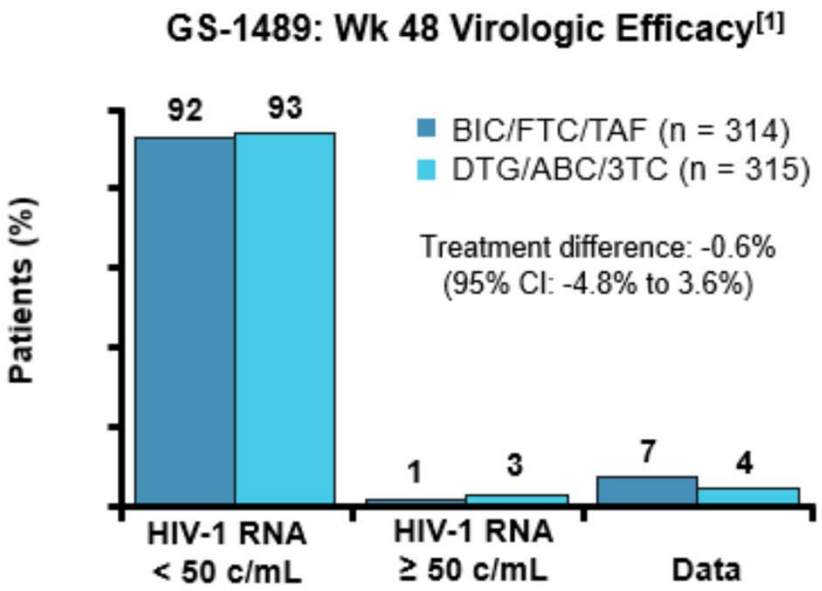
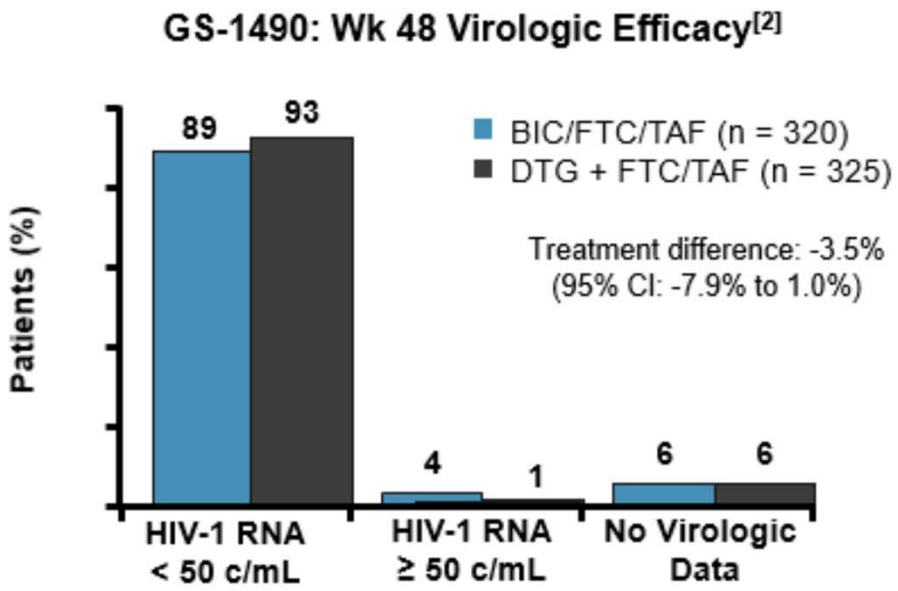
Bictegravir/Emtricitabine/Tenofovir AF vs Dolutegravir/Abacavir/Lamivudine Treatment-Naive Patients





1. Gallant J, et al. Lancet. 2017;390:2063-2072. 2. Sax PE, et al. Lancet. 2017;390:2073-2082.

Potential Risk of Dolutegravir and Neural Tube Defects

May 18, 2018:

Preliminary results from an ongoing observational study in Botswana found that women who received dolutegravir at the time of becoming pregnant or early in the first trimester appear to be at higher risk for these defects.

- weigh benefits and risks of dolutegravir in women of childbearing age.
- If using dolutegravir in persons of childbearing age, reinforce consistent use of effective birth control.
- Perform pregnancy testing before initiating a dolutegravir-containing regimen

www.fda.gov

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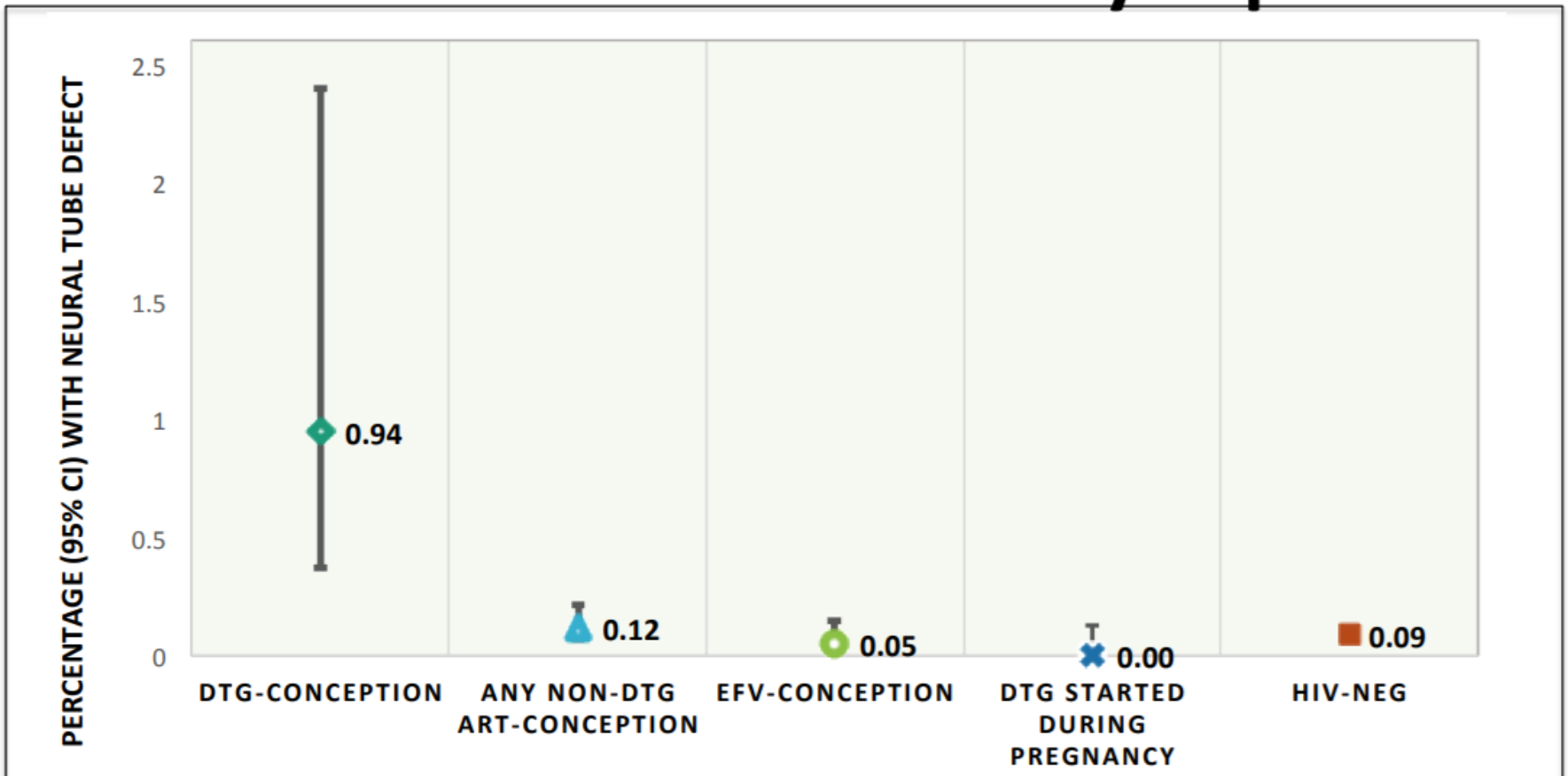
NTD Prevalence Difference by Exposure



NTDs/Exposures	4/426	14/11,300	3/5,787	0/2.812	61/66,057
% with NTD (95% CI)	0.94% (0.37%, 2.4%)	0.12% (0.07%, 0.21%)	0.05% (0.02%, 0.15%)	0.00% (0.00%, 0.13%)	0.09% (0.07%, 0.12%)
Prevalence Difference (95% CI)	**ref**	**-0.82% (-0.24%, -2.3%)**	**-0.89% (-0.31%,- 2.3%)**	**-0.94% (-0.35%, -2.4%)**	**-0.85% (-0.27%, -2.3%)**

Zash NEJM 2018 (epub 7/24/18)

Choosing Integrase Inhibitors

Agent	Advantages	Disadvantages
Bictegravir	▪ STR once daily with TAF ▪ Few interactions ▪ High barrier to resistance	▪ Only with TAF/FTC
Dolutegravir	▪ Only non-TFV QD STR ▪ High barrier to resistance ▪ Few interactions ▪ Active against RAL- and EVG -resistant viruses	▪ STR only with ABC/3TC ▪ Increases metformin levels
Elvitegravir	▪ STR once daily ▪ Available with TAF and TDF	▪ Requires COBI ▪ COBI drug interactions
Raltegravir	▪ Longest experience ▪ Few interactions	▪ Multiple pills ▪ No STR

DHHS guidelines. 2018. Dolutegravir [package insert]. 2017.

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Initial ART for PLWH

Recommended Initial Regimens in Certain 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.

• Darunavir/r or /c+Tenofovir/FTC or ABC/3TC[1]	• Efavirenz/Tenofovir/FTC
• Atazanavir/r or/c +Tenofovir/FTC or ABC/3TC [1,2]	• Raltegravir+ABC/3TC [1,2]
• Rilpivirine/Tenofovir/FTC [3]	• Darunavir/r+Raltegravir, [3]
	• Lopinavir/r+3TC

[1]HLAB5701 neg; [2] HLAB5701 neg and HIV RNA< 100,000 [3] HIV RNA < 100,000 and CD4>200

US DHHS, 2018 available at www.aidsinfo.nih.gov

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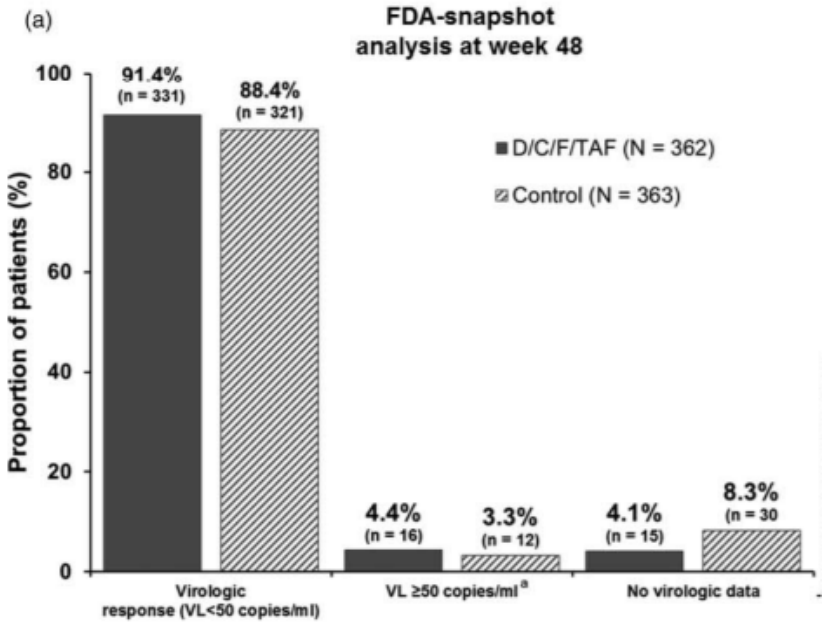
AMBER: TenofovirAF+Emtricitabine+Darunavir+Cobicistat

- Treatment naïve (n=725)
- STR (TAF/FTC/DRV/c) vs TDF/FTC + DRV/c
- Primary endpoint: Viral Load < 50 copies at week 48
- **Non-inferiority was achieved**



Eron et al. 2018, ***AIDS***

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Tenofovir AF (TAF) + Emtricitbine (FTC) + Darunavir/Cobicistat

Indications	▪ ART-naive pts ▪ Virologically suppressed
Key Drug-Drug interactions	▪ Alfuzosin, ranolazine, dronedarone, DOACs, warfarin, st john wort, statins, PD5 inhibitors, ticagrelor, rifampin, ergot derivitives ▪ Consult prescribing information for full list of DDIs
Not recommended for these populations:	▪ pts with CrCl < 30 mL/min ▪ Severe hepatic impairment (Child-Pugh Class C) ▪ Pregnancy

SYMTUZA prescribing information, 2018

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Boosted PIs in Clinical Practice

- Consider boosted PIs when **high barrier to resistance is needed**
  - If starting ART prior to availability of resistance data, if **high risk of poor adherence**
- More widely used in those with **transmitted or acquired drug resistance**

DHHS guidelines. March 2018.

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Doravirine+Emtricitabine+Tenofovir DF

- Non-nucleoside reverse transcriptase inhibitor (NNRTI) active against wild-type and common prevalent NNRTI resistance mutations (K103N, Y181C, G190A, E138K)

- Low potential for drug-drug interactions (including with acid-reducing agents)

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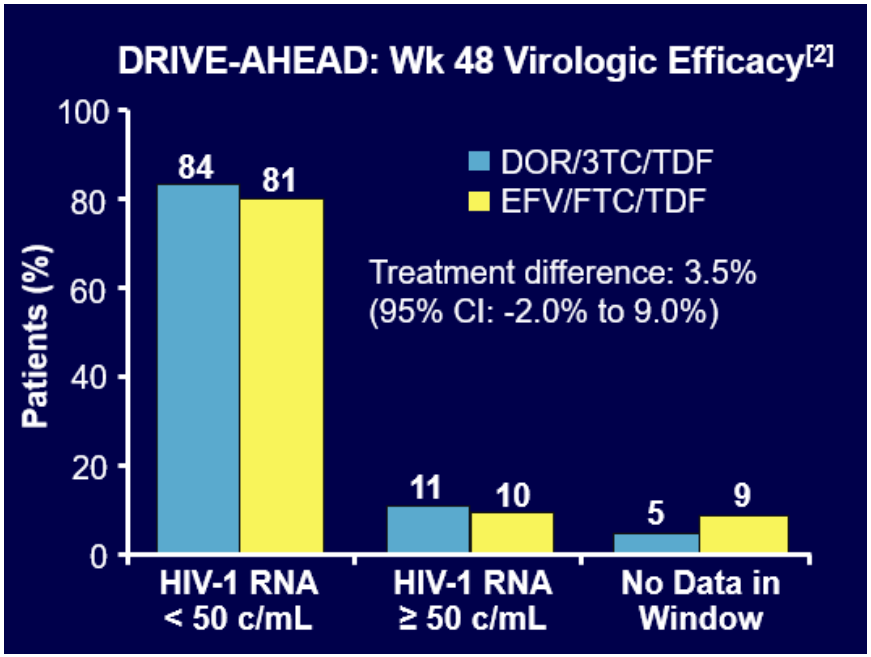
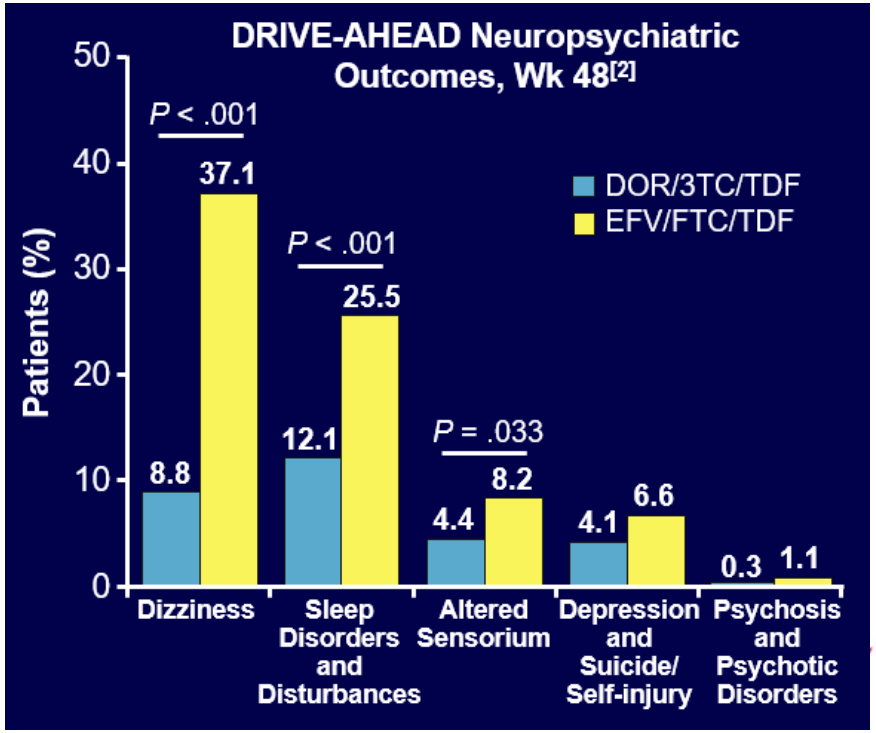
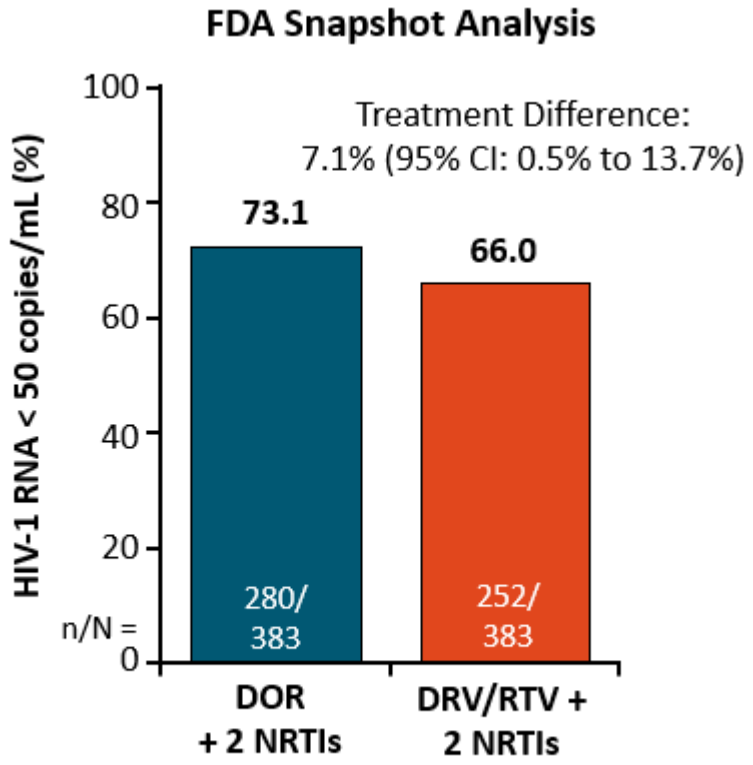
DRIVE-AHEAD:
Doravirine+Lamivudine+Tenofovir DF vs Efavirenz+Emtricitabine+Tenofovir DF

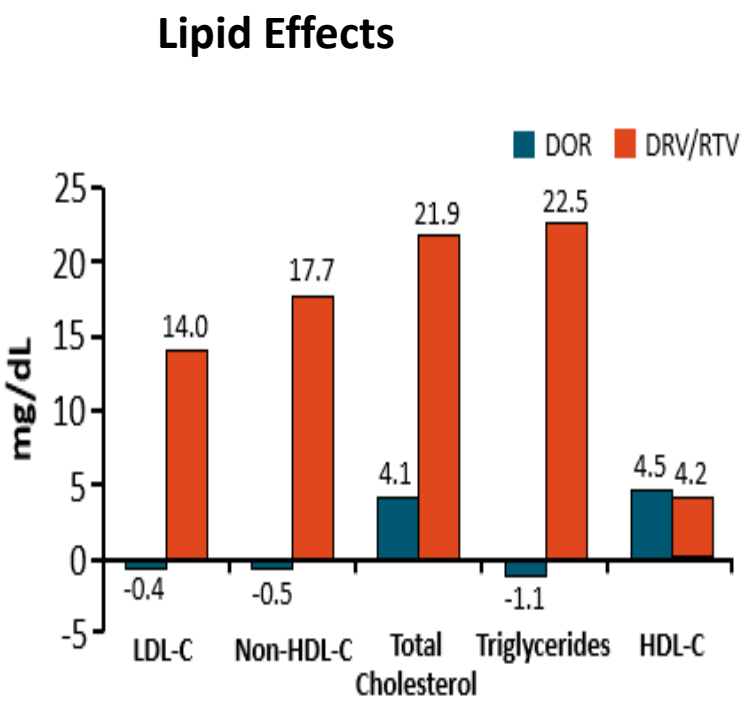




Squires et al, IAS 2017

DRIVE-FORWARD:
Doravirine+Lamivudine+Tenofovir DF vs Darunavir/r + 2 NRTIs





Molina JM, et al. AIDS 2018. Abstract LBPEB017.

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Doravirine (Pifeltro)
Doravirine+TDF+3TC (Delstrigo)

Indications	▪ ART-naive pts
Dosing	▪ One tablet once daily with or without food ▪ For patients on rifabutin, additional dose needed 12 hours after
Key Information:	▪ Do not administer DELTRIGO in pts with CrCl < 50 mL/min ▪ No drug interaction with acid reducing agents ▪ Check HBV status prior to administration of DELSTRIGO

Deltrigo and Pifeltro prescribing information, 2018

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Key Drug-Drug Interactions: Boosted PI- or NNRTI-Containing ART Regimens

Regimen	Key Drug–Drug Interactions
ATV/RTV + FTC/TDF or FTC/TAF DRV/RTV + FTC/TDF or FTC/TAF	▪ Avoid lovastatin, simvastatin, salmeterol ▪ Use caution with/avoid specific antiarrhythmics ▪ Avoid PPIs with ATV ▪ Use caution with/avoid inhaled, injected, or systemic steroids
RPV/FTC/TDF RPV/FTC/TAF DTG/RPV	▪ Avoid PPIs, dexamethasone

*Key DDIs with DTG: Dose adjust metformin (diabetes medication).

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Case Challenge #3 MK

- 67 year old, dx in 1997 who is virologically suppressed on Tenofovir AF/Emtricitabine + Nevirapine

- **Past Medical History:**
- High blood pressure, Type II Diabetes, stage III Chronic Kidney Disease (CrCl 48 mL/min)

- **Other medications**:
- Losartan-HCT 100/25mg, Metformin 1000mg BID

How would you address this situation?
What are you concerned about?

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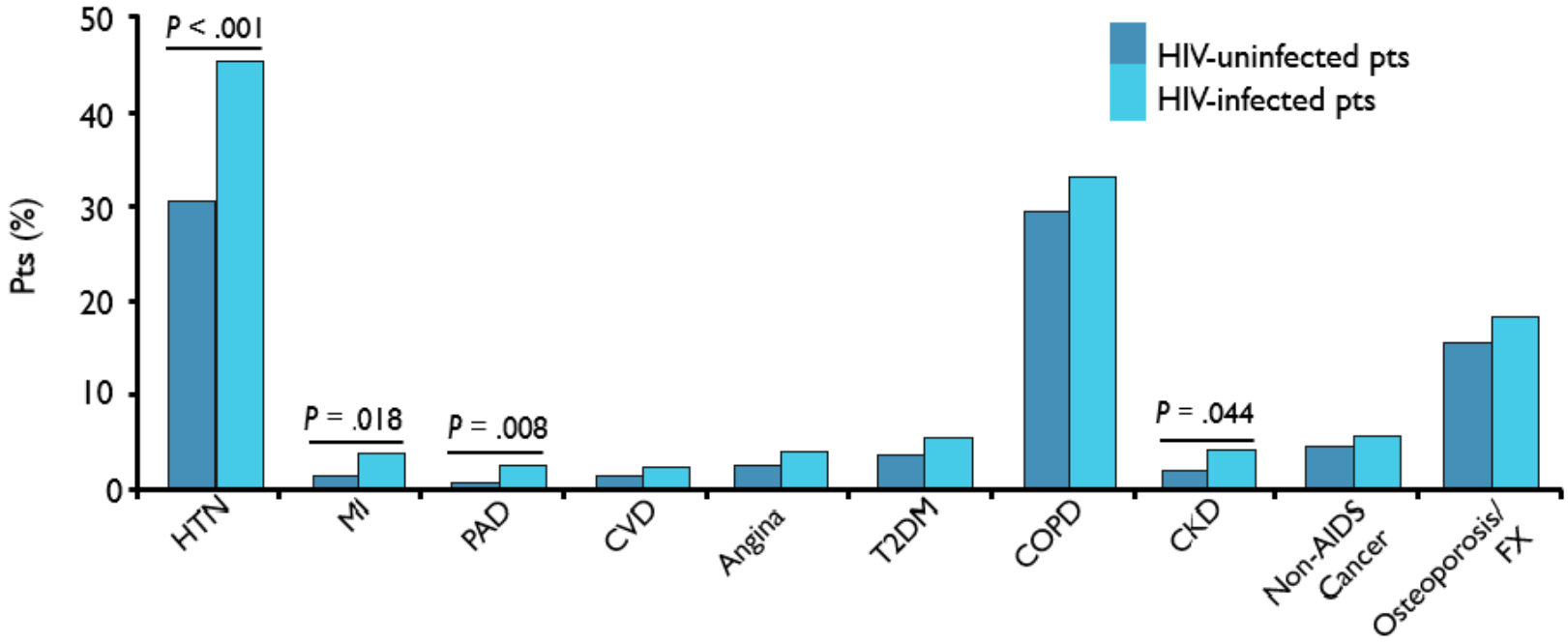
Older HIV-Infected Pts at Increased Risk for Multiple Comorbidities

- Cross-sectional analysis of comorbidity prevalence in prospective cohort study of HIV-infected pts (n = 540) vs controls (n = 524) ≥ 45 yrs of age



Schouten J. Clin Infect Dis. 2014;59:1787-1797.

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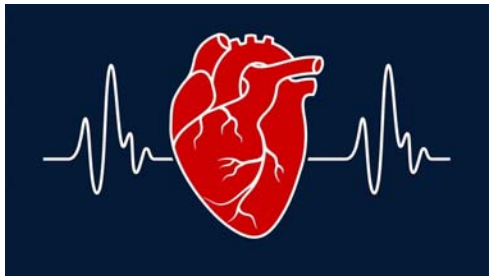
Abacavir Risk and Myocardial Infarction

- Abacavir initiators (n=1462) vs non-Abacavir initiators (n=6803)
- Abacavir was associated with **higher risk of Myocardial Infarction** (HR: **2.66** [95%CI:1.81-3.90])



Elion, R et al. 2018, Journal of acquired immune deficiency syndromes, 7891), 62-72.

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ART Considerations for Older Pts

- Greater risk of serious non-AIDS complications
- Decreased immunologic response to ART
- Adverse drug events may occur more frequently
- Polypharmacy and greater risk of drug–drug interactions

US DHHS, 2018 available at www.aidsinfo.nih.gov

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What about SWITCH Therapy?

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The Why and How of Switching in Virologic Suppression

Why

- Simplify regimen
- Tolerability
- Comorbidity
- Drug interactions
- Pregnancy
- Cost

How

- Need to consider
  - Previous ART
  - Previous resistance
  - Likelihood of adherence
  - Drug interactions
  - Comorbid conditions

US DHHS, 2018 available at www.aidsinfo.nih.gov

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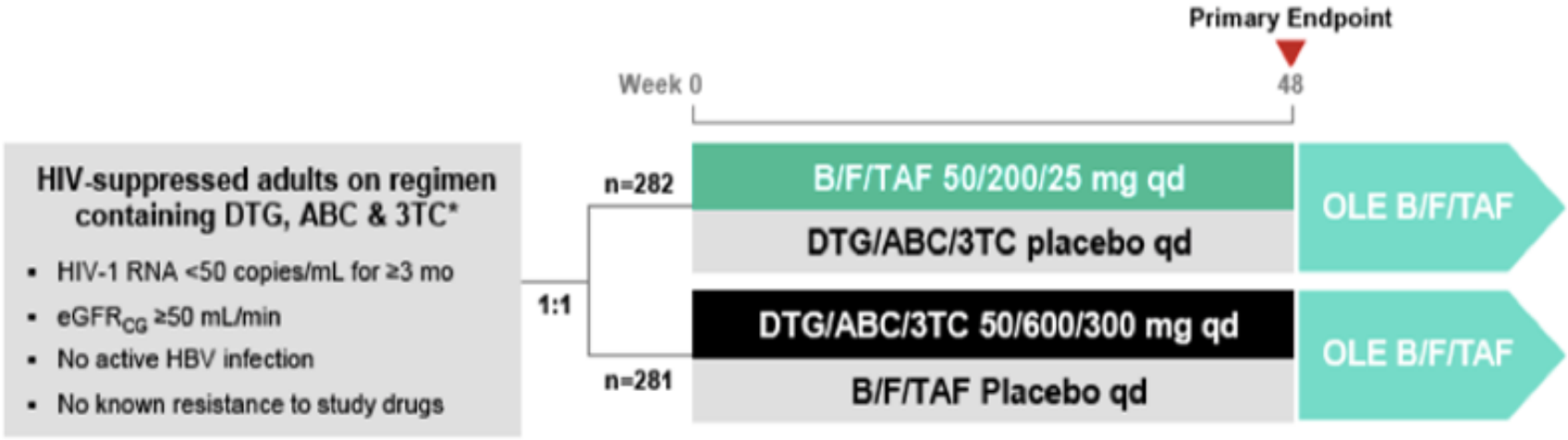
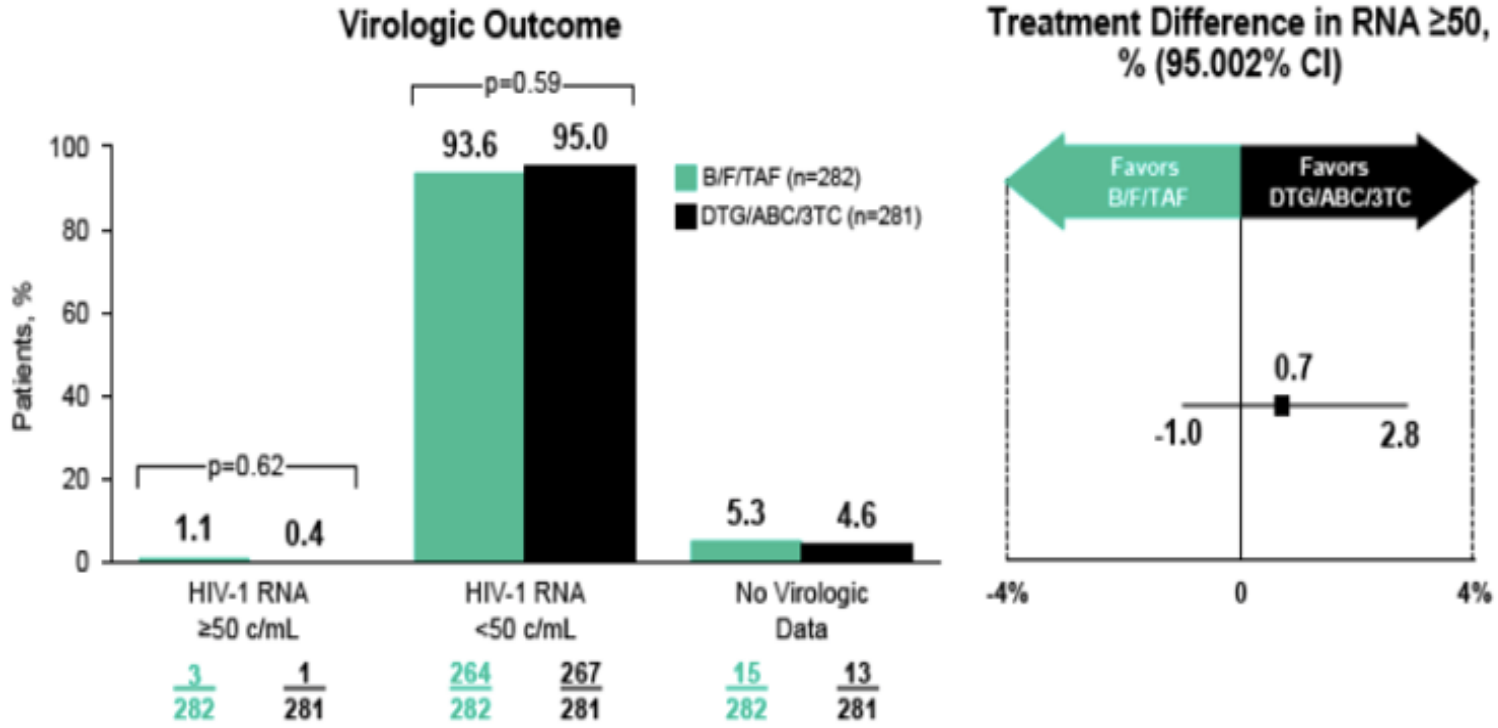
Dolutegravir/Abacavir/Lamivudine to Bictegravir/Emtricitabine/Tenofovir AF



- Phase 3, randomized, double-blind, multicenter, active-controlled study (NCT02603120): North America, Europe, Australia
- Primary endpoint: proportion with HIV-1 RNA ≥50 copies/mL at Week 48
  - Noninferiority margin of 4% based on FDA snapshot algorithm

Molina et al. CROI 2018, Abstract #22

Dolutegravir/Abacavir/Lamivudine to Bictegravir/Emtricitabine/Tenofovir AF: NON INFERIOR



B/F/TAF non-inferior to DTG/ABC/3TC

No significant differences in bone density or adverse events

Slight differences in renal function (2.8 mL/min) and triglycerides favoring B/F/TAF

Molina Abstra

Molina et al. CROI 2018, Abstract #22

Dolutegravir/Abacavir/Lamivudine to Bictegravir/Emtricitabine/Tenofovir AF: Safety Outcomes at Wk 48

Outcome, n (%)	BIC/FTC/TAF (n = 282)	DTG/ABC/3TC (n = 281)
Any AE (all grades)	225 (79.8)	225 (80.1)
AEs leading to d/c	6 (2)	2 (1)
Any TRAE	23 (8)*	44 (16)*
TRAEs†		
▪ Headache	7 (3)	8 (3)
▪ Abnormal dreams	1 (< 1)	5 (2)
▪ Flatulence	0	5 (2)
▪ Nausea	0	5 (2)
▪ Diarrhea	2 (< 1)	4 (1)
▪ Fatigue	1 (< 1)	3 (1)
▪ Insomnia	0	3 (1)
Any gr 3/4 lab abnormality	47 (17)	32 (11)
Gr 3/4 lab abnormalities‡		
▪ LDL elevation	14 (5)	13 (5)
▪ Increased amylase	7 (2)	0
▪ ALT elevation	6 (2)	0
▪ CK elevation	6 (2)	6 (2)
▪ Fasting hyperglycemia	6 (2)	2 (< 1)

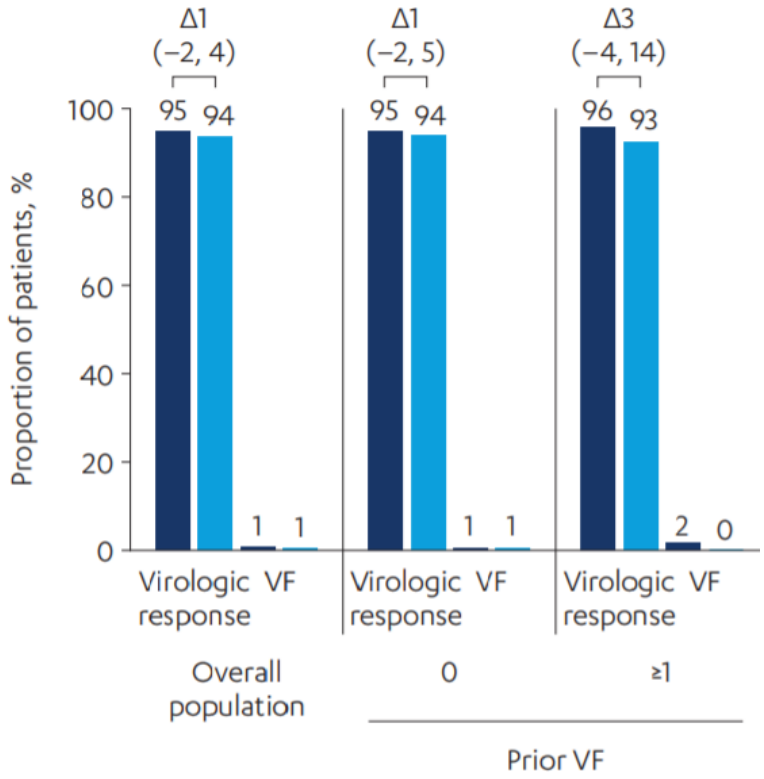
Molina et al. CROI 2018, Abstract #22

EMERALD:
Switch to Darunavir/Cobicistat/Emtricitabine/TenofovirAF in Suppressed Patients

DRV/COBI/FTC/TAF

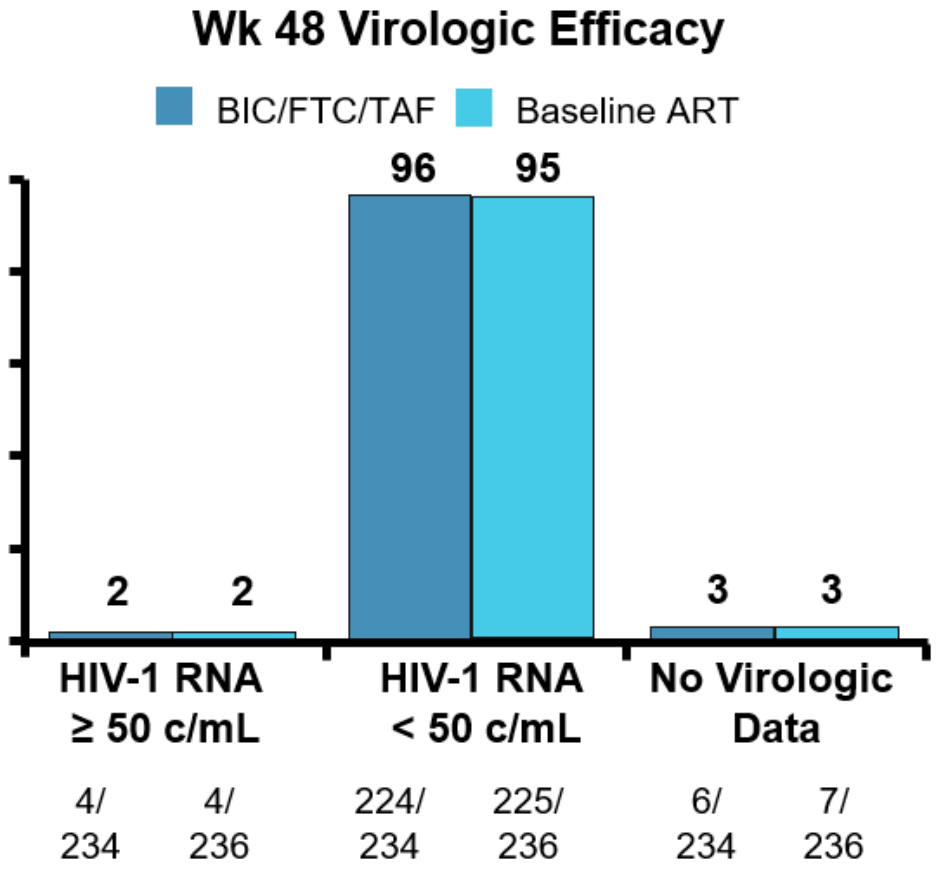
Control

D/C/F/TAF may be an effective strategy for stably suppressed individuals who would like to simplify therapy, including patients with a history of prior VF or prior experience with multiple ARVs



Eron JJ, et al. CROI 2018. Abstract 502.

Suppressive ART to Bictegravir/Emtricitabine/Tenofovir AF in Women

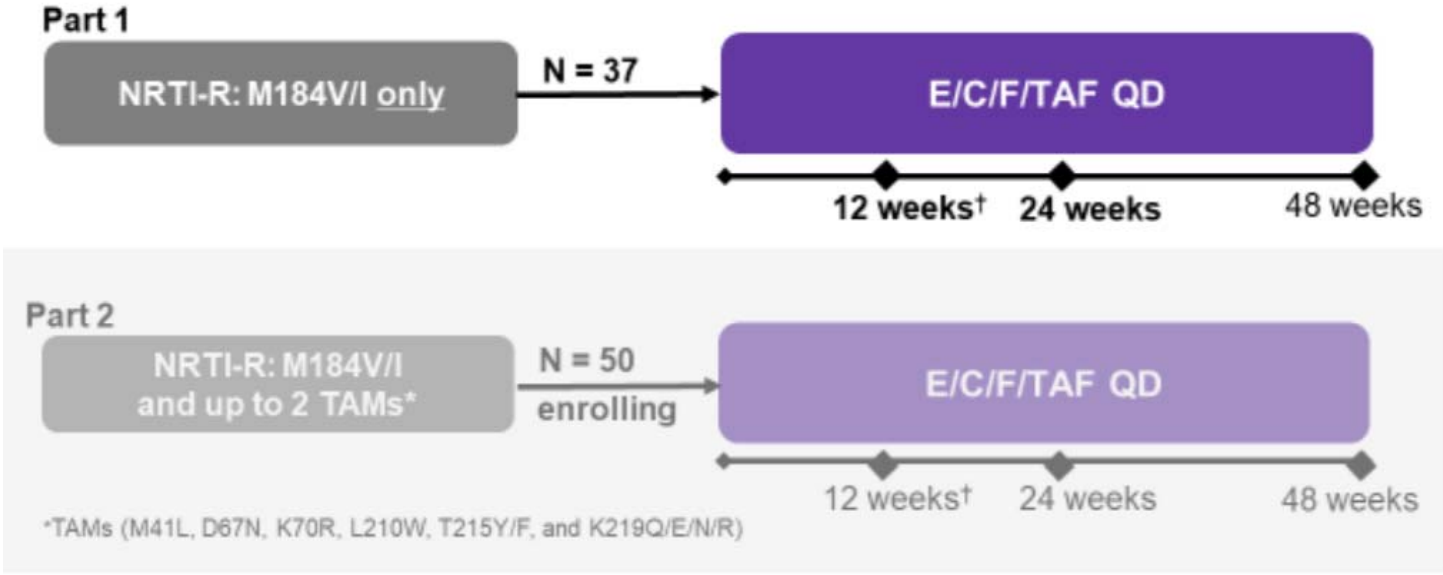


Uganda (27%), Russia (24%), Thailand (22%), US (15%), Dominican Republic (12%)

Kityo C, et al. CROI 2018. Abstract 500.

Study 1824: Switch to Elvitgravir/Cobi/Emtricitabine/Tenofovir AF in Virologically Suppressed Adults With M184V/I

Ongoing, multicenter, international, open label, single arm study in HIV-1-infected adults with HIV-1 RNA < 50 copies/mL receiving FTC/TDF or ABC/3TC + third agent



†Primary Endpoint

- HIV-1 RNA < 50 copies/mL at Week 12 using PVR (pure virologic response)

Perez-Valero I, et al. AIDS 2018. Abstract TUAB0104.

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Study 1824: Switch to Elvitgravir/Cobi/Emtricitabine/Tenofovir AF in Virologically Suppressed Adults With M184V/I

- Primary Objective
  - To evaluate the efficacy of switching to E/C/F/TAF in maintaining HIV-1 RNA < 50 copies/mL at Week 12 in participants with M184V/I using pure virologic response (PVR)
- Secondary Objectives
  - To determine the safety and tolerability of E/C/F/TAF in participants switching from 2 NRTIs + third agent
  - To evaluate the emergence of new resistance mutations in participants who develop virologic failure after switching to E/C/F/TAF
  - To determine the durability at Weeks 24 and 48 in maintaining HIV-1 RNA < 50 copies/mL using PVR

Perez-Valero I, et al. AIDS 2018. Abstract TUAB0104.

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Study 1824: Switch to Elvitgravir/Cobi/Emtricitabine/Tenofovir AF in Virologically Suppressed Adults With M184V/I

- HIV-1 RNA < 50 copies/mL at screening and for at least 6 months
  - One blip (HIV-1 RNA > 50 copies/mL) was acceptable
- Currently receiving FTC/TDF or ABC/3TC + third agent for ≥ 6 months
  - Allowable third agents included NNRTIs, PIs, RAL or DTG
- M184V and/or M184I on historical genotype
  - No exclusionary PI, NRTI or INSTI mutations on historical genotype
  - No additional exclusionary mutations seen on proviral DNA genotype (done at screening on all participants)
- No prior virologic failure on PI or INSTI-based regimen
- Estimated GFR ≥ 30 mL/min (Cockcroft-Gault formula)

Perez-Valero I, et al. AIDS 2018. Abstract TUAB0104.

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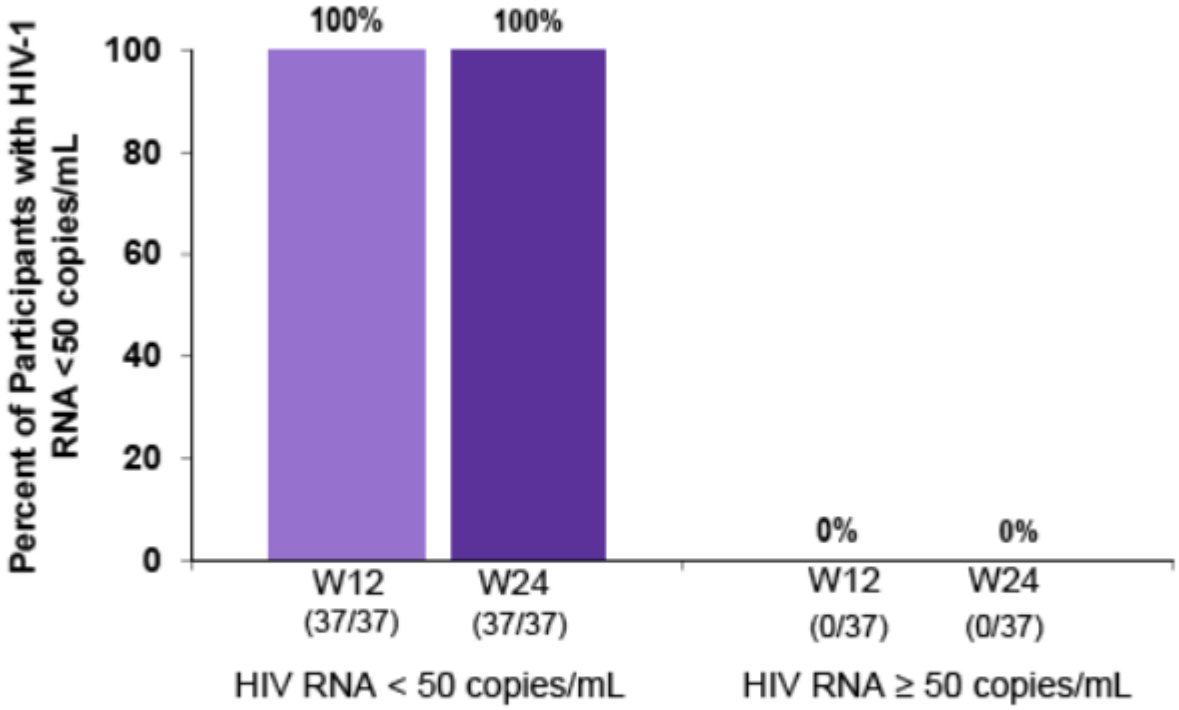
Study 1824: Switch to Elvitgravir/Cobi/Emtricitabine/Tenofovir AF in Virologically Suppressed Adults With M184V/I

	E/C/F/TAF n=37
Median age, years (range)	51 (22-76)
Female	8 (22%)
Race/ethnicity	
White	27 (73%)
Black or African descent	7 (19%)
Hispanic/Latino ethnicity	6 (16%)
HIV-1 RNA <50 copies/mL, baseline	37 (100%)
Median CD4 count, cells/mm^3 (range)	724 (143-1503)
CD4 <200 cells/mm^3	1 (3%)
Median estimated GFR_{CG}, mL/min (range)	94 (36-215)
Screening Regimen: Third Agents*	
NNRTI	11%
INSTI	32%
PI	54%
Screening Regimen: FTC/TDF as NRTI backbone	54%

*2 participants included in analyses had non-allowable third agents in screening regimen (E/C/F/TDF and FTC/TDF+ETR+RAL)

Perez-Valero I, et al. AIDS 2018. Abstract TUAB0104.

Pure Virologic Response (HIV RNA < 50 copies/mL) at Week 12 and Week 24



Two participants each experienced a single viral blip (69 and 93 copies/mL)

Week 12 (Primary) and Week 24 PVR Analyses:

- No virological failures or emergence of new resistance

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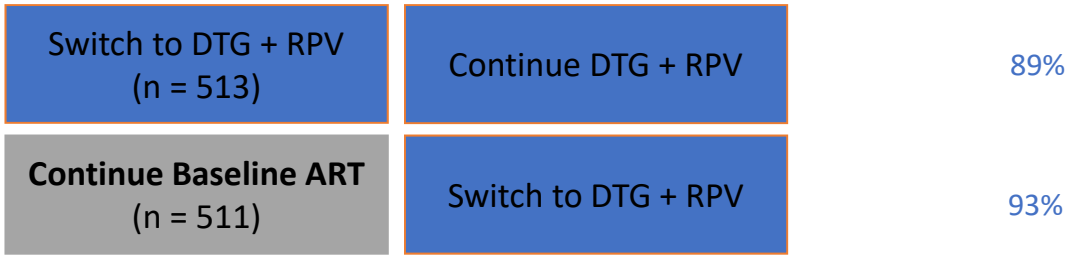
SWORD-1 and -2: Switch to DTG + RPV vs Continuation of Baseline ART in Virologically Suppressed Adults

- Parallel, randomized, open-label, multicenter phase III noninferiority studies[1,2]



- Primary endpoint: HIV-1 RNA < 50 copies/mL maintained in 95% of patients in each arm at Wk 48; adjusted treatment difference: -0.2% (95% CI: -3.0 to 2.5)[2]

1. Aboud M, et al. AIDS 2018. Abstract THPEB047. 2. Llibre JM, et al. Lancet. 2018;391:839-849.

Slide credit: clinicaloptions.com

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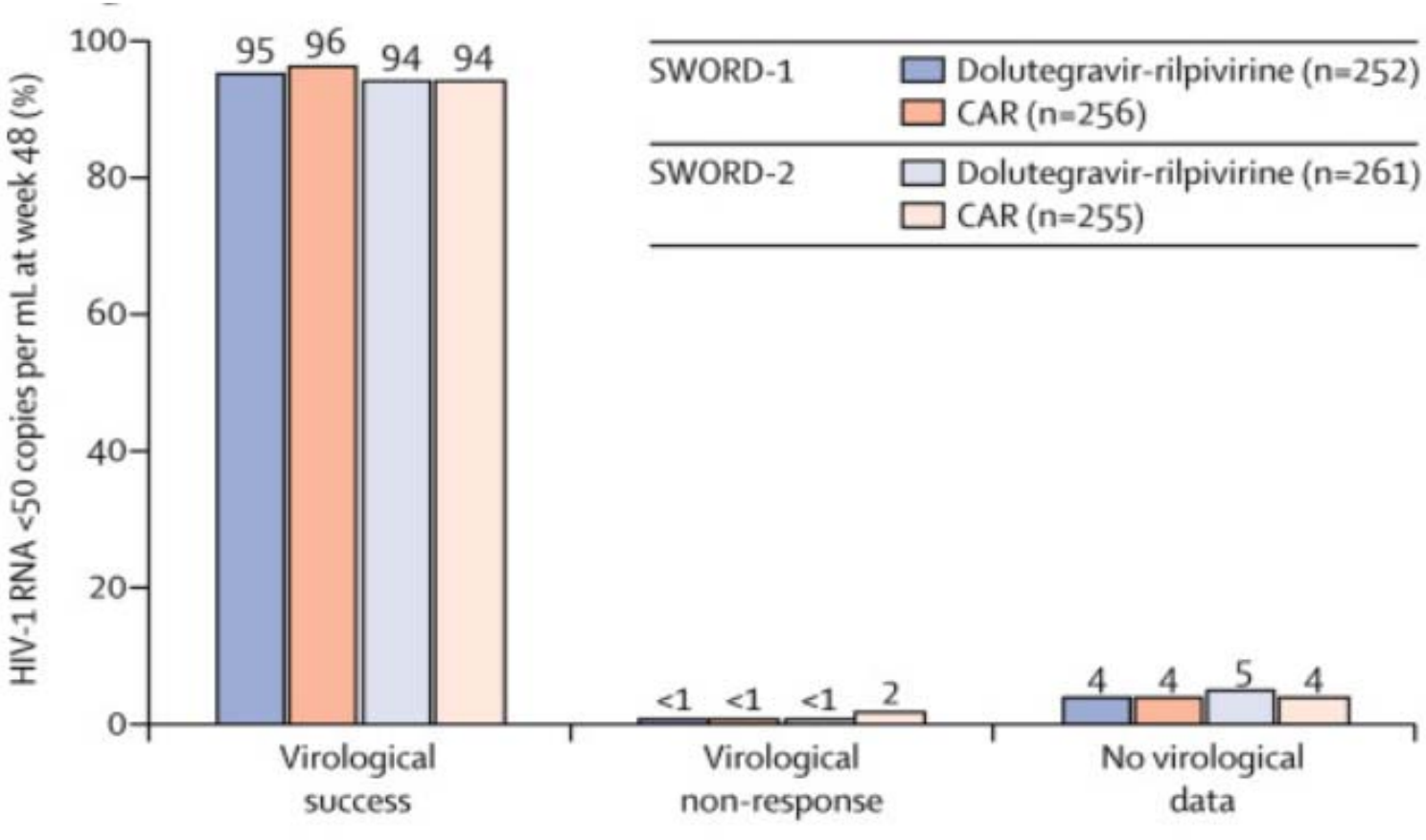
Dolutegravir/Rilpivirine
SWORD-1 and SWORD-2
Patients with no previous history of Virologic Failure



Llibre JM, et al. Lancet. 2018;391:839-849.

Dolutgravir/Rilpivirine for Maintenance Therapy

Key US Label Information	
Indication	▪ Virologically suppressed for ≥ 6 mos ▪ No history of treatment failure or resistance to DTG or RPV
Administration requirements	▪ Must be taken with a meal
Key DDIs	▪ Separate dose of DTG/RPV and antacid/polyvalent cation–containing medications ▪ Avoid PPIs
Dose adjustments	▪ None for patients with mild/moderate renal impairment; ▪ Patients with CrCl < 30 mL/min, increase monitoring for AEs

DTG/RPV [package insert]. 2018. DHHS guidelines. March 2018.

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DUAL-GESIDA 8014: Darunavir/ritonavir + Lamivudine From Triple Therapy

- Open-label, randomized, noninferiority trial of suppressed patients switched to DRV/RTV + 3TC or continued DRV/RTV + ABC/3TC or FTC/TDF
- DRV/RTV + 3TC **noninferior to triple therapy for maintenance** of suppression through 48 wks

Outcome at Wk 48	Switch to Dual Therapy (n = 126)	Continue Triple Therapy (n = 123)
HIV RNA < 50 c/mL (ITT FDA Snapshot),* %	89	93
HIV RNA < 50 c/mL in all study visits, %	83	83

*Treatment difference: -3.8 (95% CI: -11 to 3.4).

Pulido F, et al. Clin Infect Dis. 2017;65:2112-2118.

Guidance for Switching to Dual Therapy in Virologically Suppressed Patients

With Evidence

- **DTG + RPV** a reasonable option when use of NRTIs not desirable and when no expected resistance to regimen components
- **PI/RTV + 3TC** may be a reasonable option when use of TDF, TAF, or ABC is contraindicated or not desirable

Without Evidence

Insufficient evidence to recommend:

- DTG + 3TC,
  DRV/RTV + RAL

***Not recommended*:**

- DTG or PI/RTV monotherapy,
- ATV/RTV + RAL

DHHS guidelines. March 2018.

Ibalizumab

- A long-acting, nonimmunosuppressive mAb, CD4-directed post-attachment HIV-1 inhibitor: blocks HIV entry into CD4 cells
  - In combination with other ARV(s), indicated for the treatment of HIV-1 infection in *heavily treatment-experienced adults with multidrug-resistant HIV-1 infection*, who are failing their current ARV regimen
  - Administered IV as a single loading dose of 2000 mg followed by a maintenance dose of 800 mg every 2 wk (dilution in 250 mL of 0.9% sodium chloride injection, USP)

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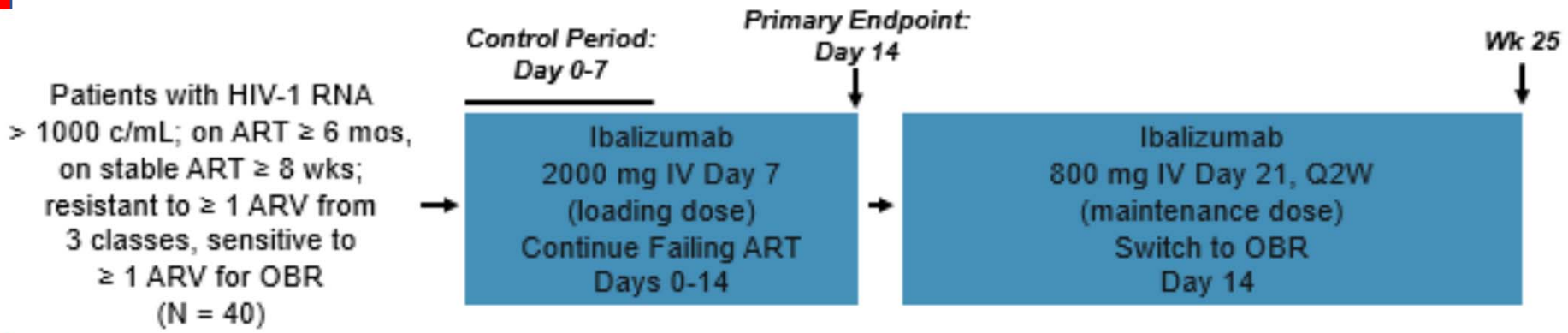
TMB-301: Ibalizumab



Trogarzo PI (2018).

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Ibalizumab Study TMB-301: Virologic Outcomes

	Subjects achieving <50 HIV-1 RNA copies/mL (%)		Subjects achieving <200 HIV-1 RNA copies/mL (%)	
CD4 Cell Counts		(n)		(n)
<50 (n=17)	18	**(3)**	24	**(4)**
50-200 (n=10)	60	**(6)**	70	**(7)**
>200 (n=13)	62	**(8)**	69	**(9)**
Viral Load				
≤100,000 (n=33)	49	(16)	58	(19)
>100,000 (n=7)	14	(1)	14	(1)
Resistance				
With INSTI Resistance (n=27)	41		44	
Without INSTI Resistance (n=13)	46		62	

Trogarzo PI (2018).

Ibalizumab Study TMB-301: Adverse Events

Selected Laboratory Abnormalities (≥ Grade 3) in Trial TMB-301

	% Subjects N=40
Bilirubin (≥ 2.6 x ULN)	5%
Direct Bilirubin (> ULN)	3%
Creatinine (> 1.8x ULN or 1.5x baseline)	10%
Blood Glucose (> 250 mg/dL)	3%
Lipase (> 3.0 x ULN)	5%
Uric Acid (> 12 mg/dL)	3%
Hemoglobin (< 8.5 g/dL)	3%
Platelets (< 50,000/mm^3)	3%
Leukocytes (< 1.5 10^9 cells/L)	5%
Neutrophils (< 0.6 10^9 cells/L)	5%

	N=40
Diarrhea	8%
Dizziness	8%
Nausea	5%
Rash*	5%

Trogarzo PI (2018).

Novel Strategies

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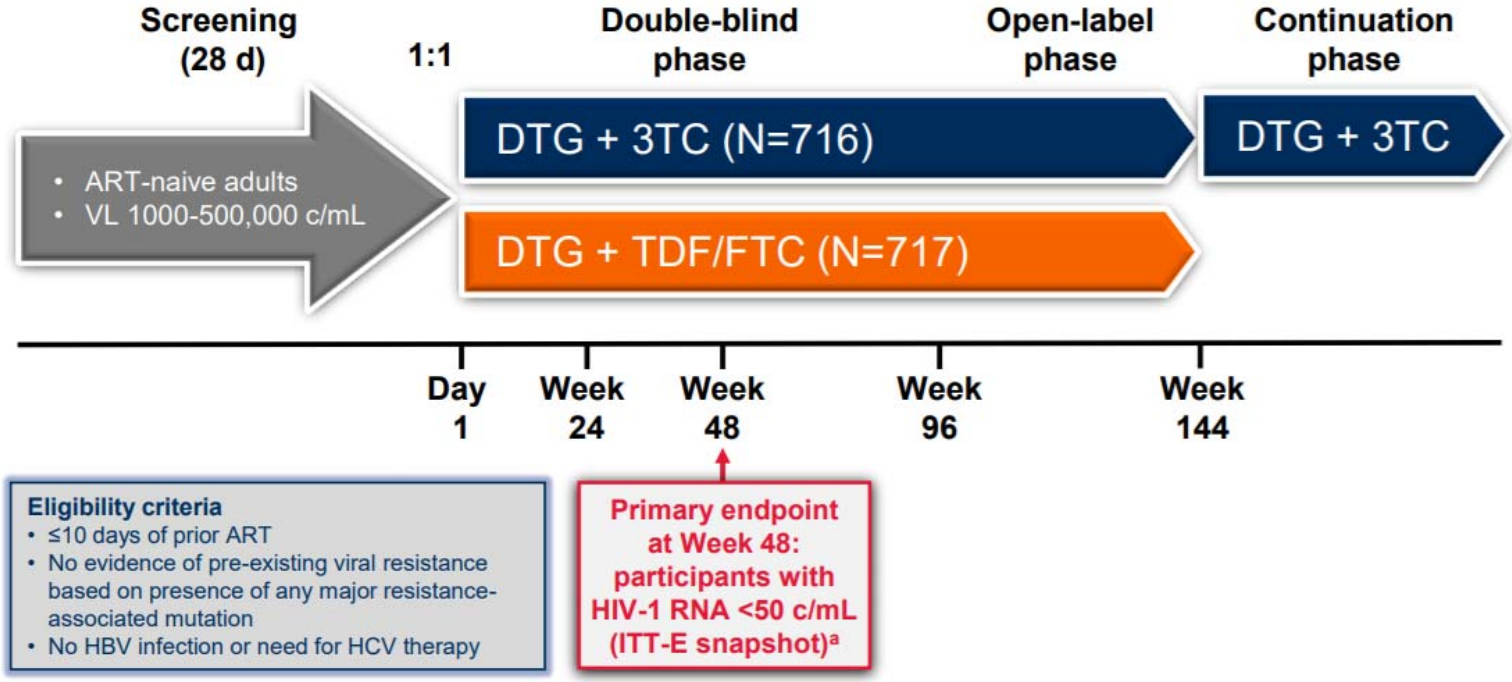
GEMINI Study: Dolutegravir+Lamivudine vs Dolutegravir+Tenofovir DF+Emtricitabine in Treatment Naïve Adults

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



Cahn AIDS 2018 #TUAB0106LB

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GEMINI Study: Dolutegravir+Lamivudine vs Dolutegravir+Tenofovir DF+Emtricitabine in Treatment Naïve Adults

Characteristic	DTG + 3TC (N=716)	DTG + TDF/FTC (N=717)
Age, median (range), y	32.0 (18-72)	33.0 (18-70)
≥50 y, n (%)	65 (9)	80 (11)
Female, n (%)	113 (16)	98 (14)
Race, n (%)		
African American/African heritage	99 (14)	76 (11)
Asian	71 (10)	72 (10)
White	480 (67)	497 (69)
Other	66 (9)	72 (10)
Ethnicity, n (%)		
Hispanic or Latino	215 (30)	232 (32)
Not Hispanic or Latino	501 (70)	485 (68)
HIV-1 RNA, median (range), log_{10} c/mL	4.43 (1.59-6.27)	4.46 (2.11-6.37)
≤100,000	576 (80)	564 (79)
>100,000[a]	140 (20)	153 (21)
CD4+ cell count, median (range), cells/mm^3	427.0 (19-1399)	438.0 (19-1497)
>200	653 (91)	662 (92)
≤200	63 (9)	55 (8)

[a]2% of participants in each arm had baseline HIV-1 RNA >500,000 c/mL

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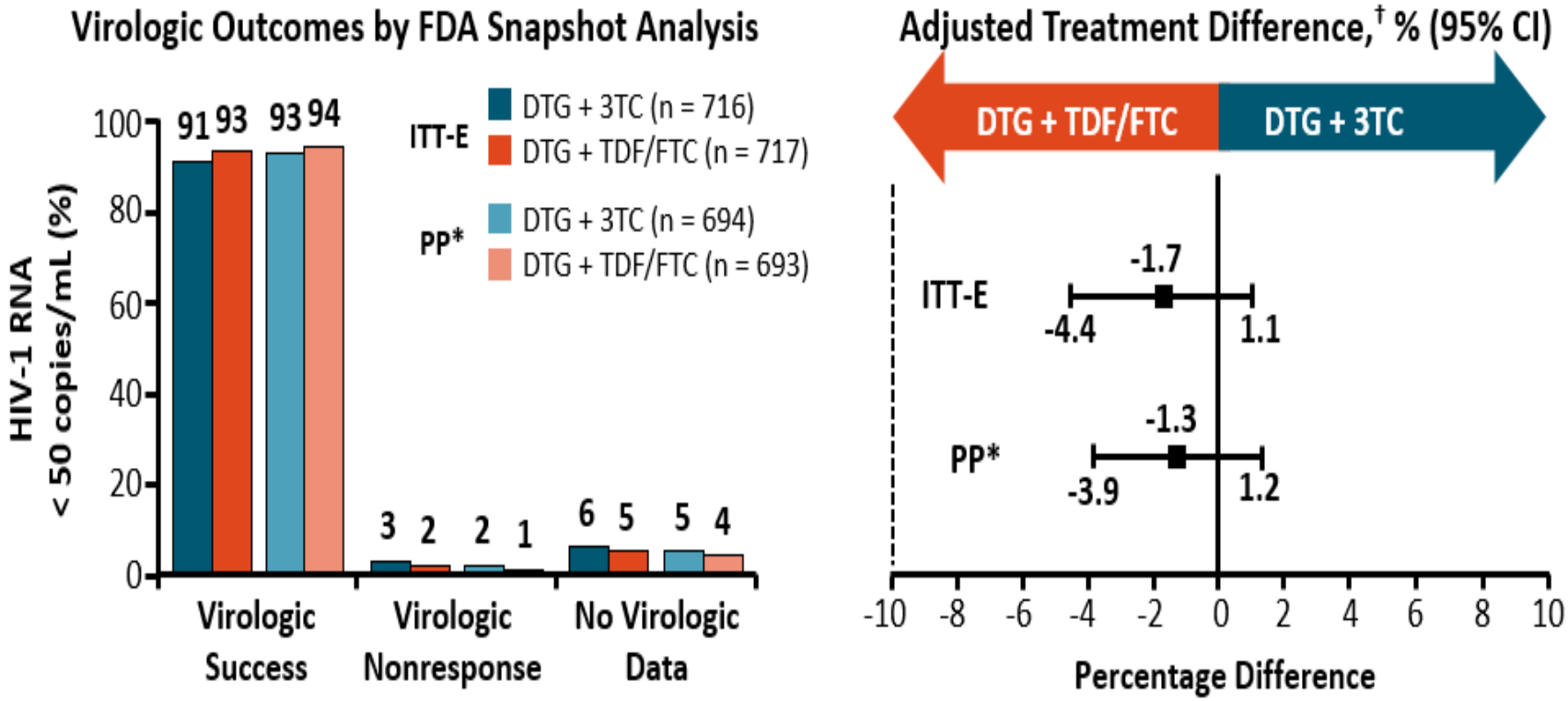
GEMINI Study: Dolutegravir+Lamivudine vs Dolutegravir+Tenofovir DF+Emtricitabine in Treatment Naïve Adults



*ITT-E population excluding significant protocol violations.

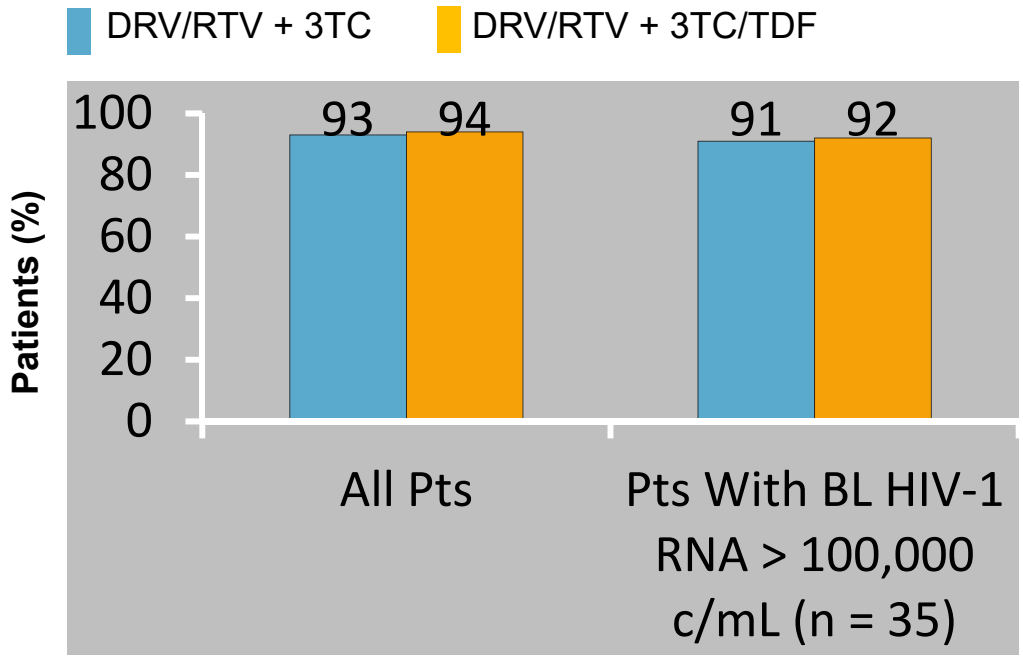
†Adjusted for HIV-1 RNA (≤ vs > 100,000 copies/mL), CD4+ cell count (≤ vs > 200 cells/mm³), and study (GEMINI-1 vs GEMINI-2).

GEMINI Study: Dolutegravir+Lamivudine vs Dolutegravir+Tenofovir DF+Emtricitabine in Treatment Naïve Adults

- **Resistance**
  - Virologic failure: n=6 (2-drugs) vs. n=4 (3-drugs)
  - No resistance to INSTI or NRTI emerged in either arm
- **Adverse events**
  - Both arms: 10% headache (1% drug-related)
  - 2% AE withdrawal each arm (wide ranging reasons)
  - 7-8% SAE, 2 deaths (1 each arm, not drug-related)
  - CKD-EPI eGFR declined significantly more in TDF arm
- **Renal & bone markers**
  - Improved renal biomarkers (uPCR, RBP, B2M) in 2D arm, statistically significant increase in 3D arm
  - No change bone biomarkers 2D arm, statistically significant increase in 3D arm (bsALP, OC, PINP)

ANDES: DRV/RTV + 3TC vs DRV/RTV + 3TC/TDF in Treatment-Naive Patients at Wk 48

ART-naive patients with HIV-1 RNA > 1000 c/mL, no NRTI or PI resistance, and HBsAg negative (N = 145)

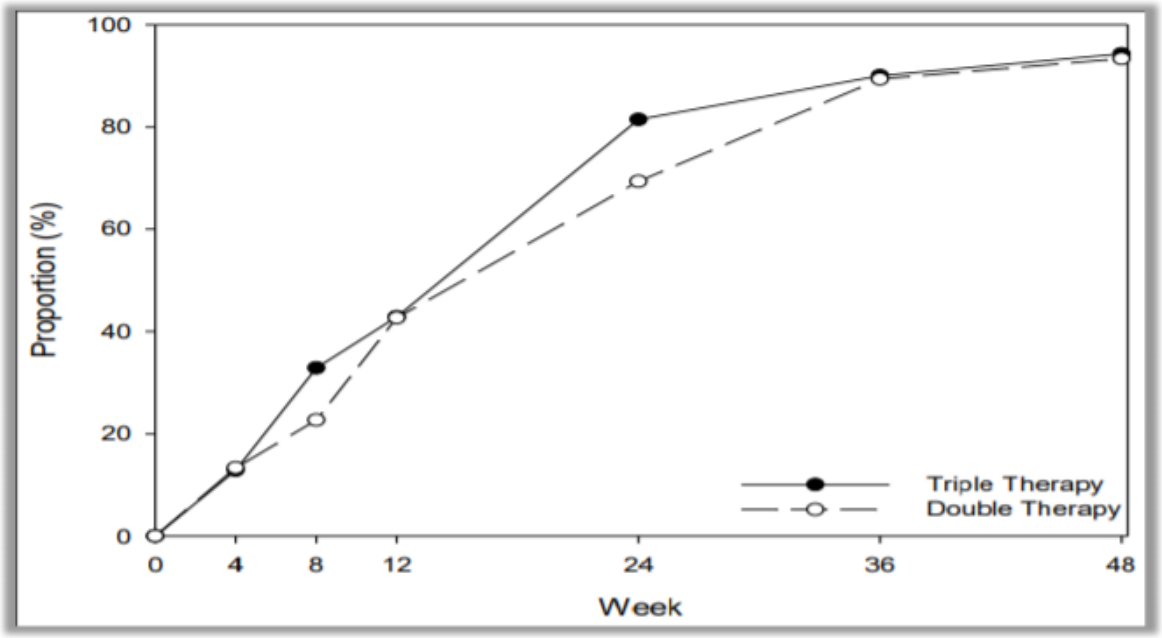


Figueroa MI, et al. CROI 2018. Abstract 489.

ANDES: DRV/r+3TC for Treatment Naive

Similar Outcomes in Dual Therapy vs Triple Therapy

Figure 1. Proportion of patients with plasma HIV-1 RNA less than 50 copies/mL



N=75 (Dual) N=70 (Triple)

Figueroa, CROI 2018, Abstract #489

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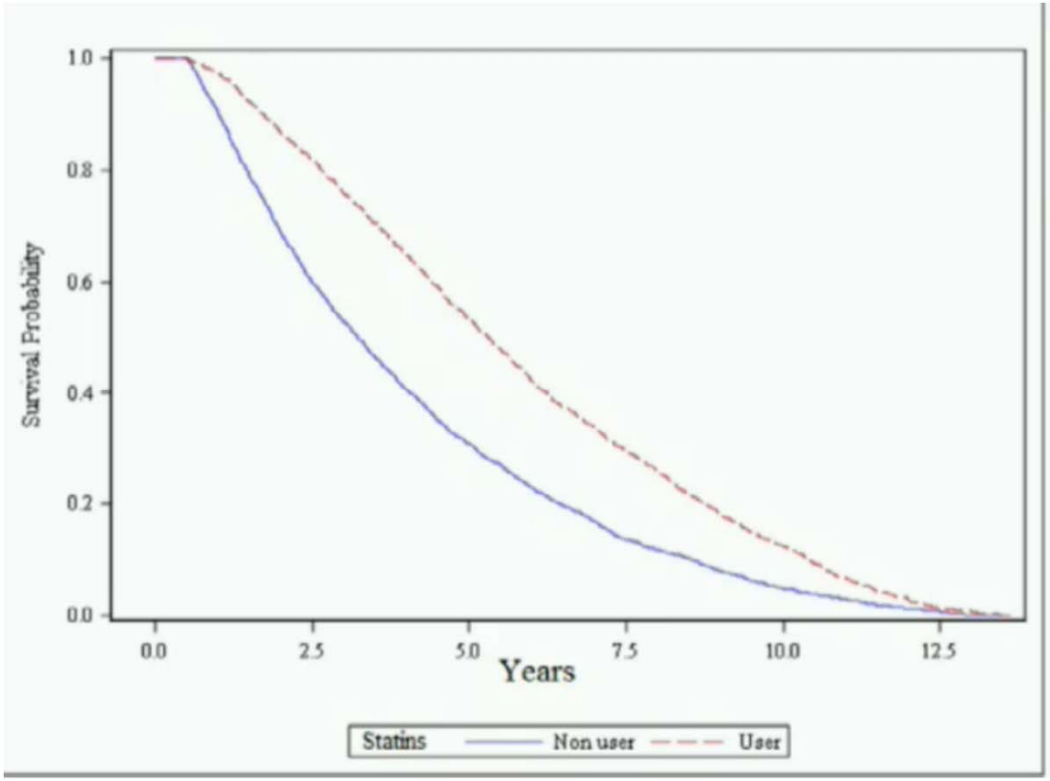
Statin Exposure and Mortality (VACS Cohort)



- Incident deaths: n=4,431
- HR for statin use: 0.55 (0.50 – 0.62)

Death rate 45% lower with statin use

Bedimo et al. CROI 2018, Abstract 132

Impact of Statin Exposure on Cancer in Older Patients With HIV Infection

- Findings
  - Incident cancers diagnosed in 940 (9.7%) of 9649 HIV+ and 3079 (8.0%) in 38,565 uninfected persons
  - Statin use associated with ~20% reduced risk of any cancer (HR 0.82 [95% CI: 0.77, 0.88]) and ~40% lower risk for infection-related cancers, eg, cervical, anal, oral (HR 0.62 [95% CI: 0.55, 0.70])
  - Association stronger in HIV+ persons but not statistically significant, except for non-Hodgkin lymphoma
- Conclusion
  - Statin exposure is associated with lower risk of cancer, independent of HIV status
  - Statins are underprescribed

Bedimo R, et al. CROI 2018. Abstract 132.

Substance Use in MSM and PLWH

- Assessed psychoactive substance use, cigarette smoking, and excessive drinking in 1018 individuals (76.8% male)
- During prior 3 months, 37.8%reported substance use, 22% excessive ETOH, 44.6% cigarette use.
- Substance Use > in MSM vs heterosexual men
- Tobacco use, being on opioid maintenance therapy, MSM correlated with higher viral loads.

Take Home:

Screening was well received. Recommend incorporating screening into routine clinical care for PLWH

Jacquet et al., AIDS: April 19, 2018 - Volume Publish Ahead of Print - Issue - p

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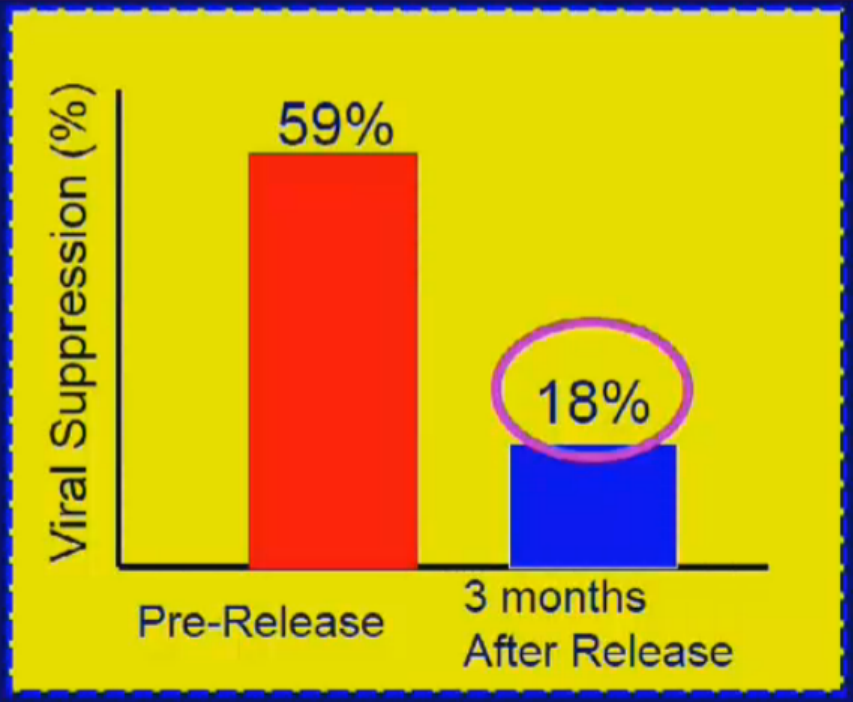
HIV Viral Suppression Lost Quickly after Release from Prison to the Community & the Public Health Importance



1. Springer et al, *Clin Infect Dis*. 2004.

- Relapse to drug & alcohol use occurs quickly after release[2,3] & is associated with loss of Viral Suppression (VS)[1,8]
- Loss of VS is associated with:
  - ↑ morbidity [4]
  - ↑transmission of HIV [5,6,7]

2. Kinlock, JSAT 2002.; 3. Springer et al CID , 2011.;
4. DHHS Guidelines Initiation of ART in PLH. 2017;
5. Anderson, Nature, 1988; 6.Hollingsworth, JID, 2008;
7. Cohen NEJM, 2011; 8. Meyer et al., Lancet, 2014.

Use of Naltrexone Improves Viral Suppression

- NEW HOPE, (n=93) for Opioid Use Disorder
- INSPIRE, (n=100) Alcohol Use Disorder

- Randomized 2:1 to receive 6 monthly injections of XR-NTX or placebo starting one week prior to release and continuing for 6 months post-release.

Springer, CROI 2018, Abstract 96

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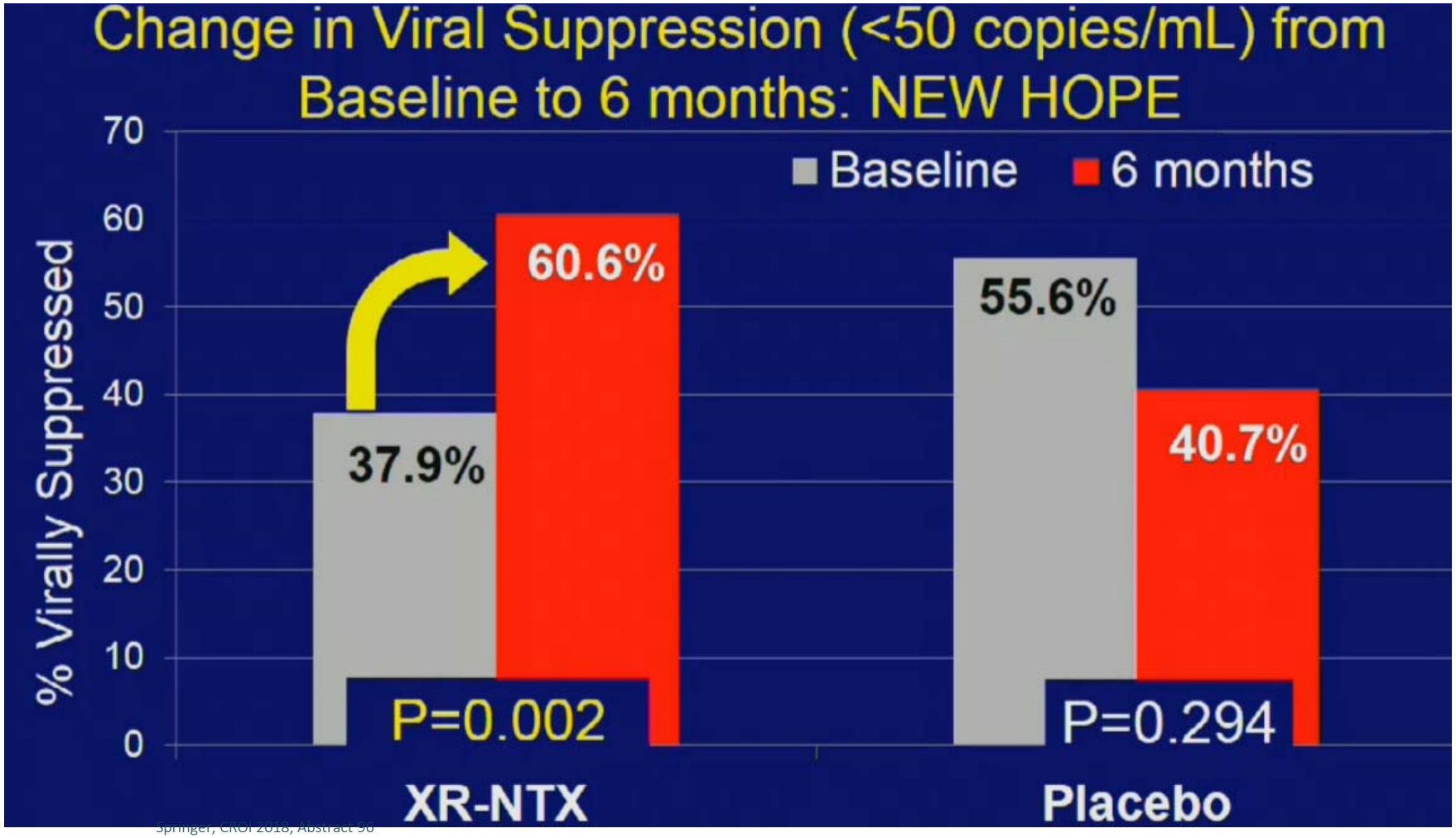
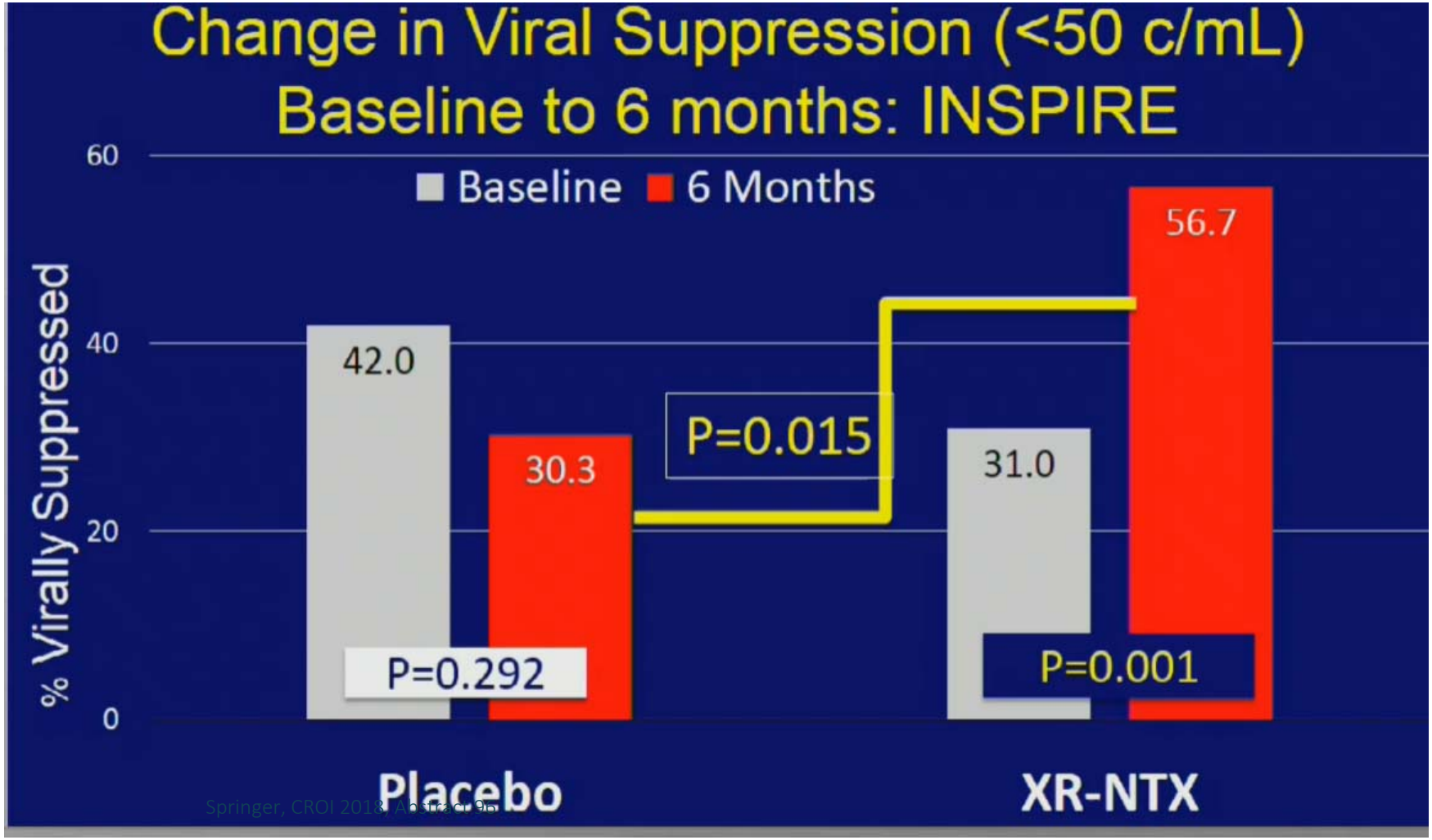


Springer, CROI 2018, Abstract 96



Springer, CROI 2018 | Abstract 96

Summary

- **Integrase-based therapies** are now considered **preferred agents** for ART naïve patients
- **Rapid ART therapy** is associated with improved outcomes
- **Newer ART strategies** and delivery modalities may reduce side effects, improve adherence, and **provide other options for virologic suppression**.
- **Co-morbidities,** including cardiovascular disease, malignancies, TB, and substance use **must continually be addressed** as the epidemic evolves.

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THANK YOU

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