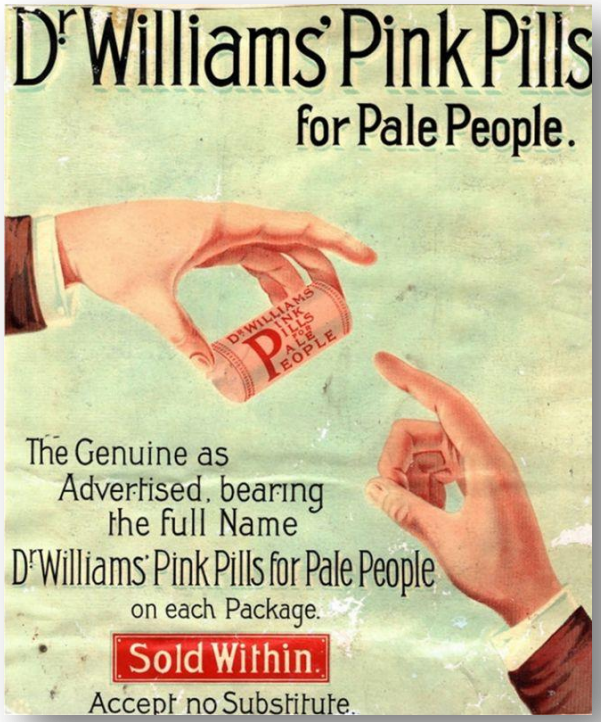
ART: What to Start and When to Switch



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What We're Starting Now

DHHS Guidelines, July 2016: What to Start

Recommended regimens	
PI based	▪ DRV/r + (TDF/FTC or TAF/FTC)
INSTI based	▪ DTG + (TDF/FTC or TAF/FTC) ▪ DTG/ABC/3TC ▪ EVG/c/TDF/FTC or EVG/c/TAF/FTC ▪ RAL + (TDF/FTC or TAF/FTC)
Alternative regimens	
NNRTI based	▪ EFV/TDF/FTC or EFV + TAF/FTC ▪ RPV/TDF/FTC or RPV/TAF/FTC (VL <100,000; CD4 >200)
PI based	▪ (ATV/c or ATV/r) + (TDF/FTC or TAF/FTC) ▪ (DRV/c or DRV/r) + ABC/3TC ▪ DRV/c + (TDF/FTC or TAF/FTC)

DHHS Guidelines for Antiretroviral Therapy in Adults and Adolescents, July 2016.

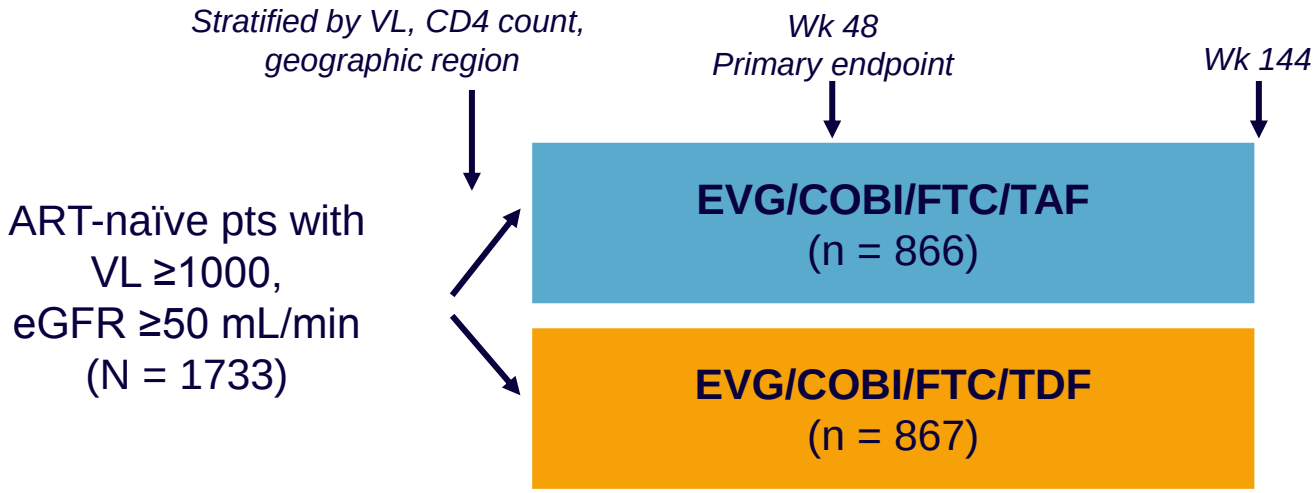
IAS–USA Guidelines, July 2016: What to Start

Recommended Regimens
▪ DTG/ABC/3TC ▪ DTG + FTC/TAF ▪ EVG/c/FTC/TAF ▪ RAL + FTC/TAF
Regimens When INSTIs Are Not an Option
▪ DRV/c or DRV/r + (FTC/TAF, FTC/TDF or ABC/3TC) ▪ EFV/FTC/TDF ▪ RPV/FTC/(TAF or TDF)

Günthard HF, et al. *JAMA* 2016;316:191-210.

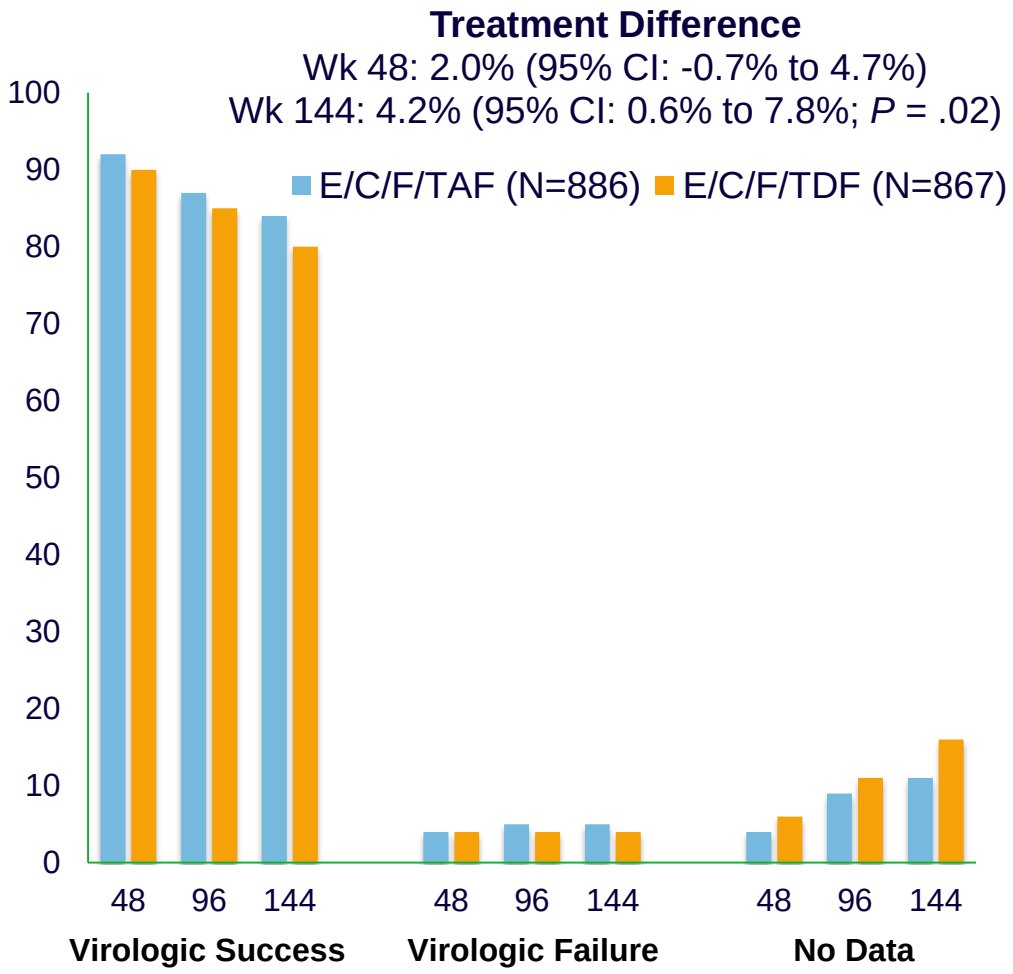
GS 104/111:
Initial ART with E/C/F/TAF vs E/C/F/TDF

- Parallel, randomized, double-blind, active-controlled phase III studies
  - 1º endpoint: VL <50 at Wk 48 (FDA Snapshot)



Arribas JR, et al. CROI 2017. Abstract 453. Sax PE, et al. *Lancet*. 2015;385:2606-2615.

Initial ART with E/C/F/TAF vs E/C/F/TDF: 144 Week Efficacy



- Efficacy similar across subgroups, trending toward or significantly better with TAF in each group
  - By baseline VL, baseline CD4, adherence, age, sex, race, region
- Virologic failure with resistance by Wk 144: 1.4% in each arm

Arribas JR, et al. CROI 2017. Abstract 453. Sax PE, et al. Lancet. 2015;385:2606-2615.

Initial ART With E/C/F/TAF vs E/C/F/TDF: 144-Week Safety Outcomes

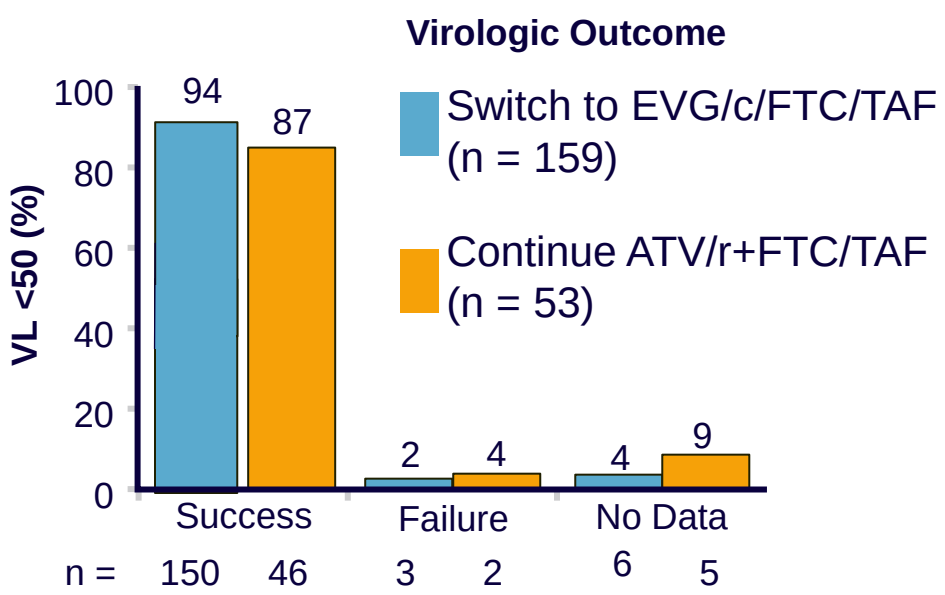
- More discontinuation for AEs with TDF vs TAF
  - 3.3% vs 1.3% (*P* = .01)
- Greater spine and hip BMD loss with TDF vs TAF
  - 6 D/Cs for bone AEs in TDF arm vs 0 in TAF arm
- TC, LDL, and HDL increases greater with TAF vs TDF
  - Rates of lipid-modifying therapy initiation similar: 5.5% vs 5.8%
- Med. eGFR increase lower with TAF vs TDF regimen: 1.6 vs 7.7 mL/min (*P* < .001)

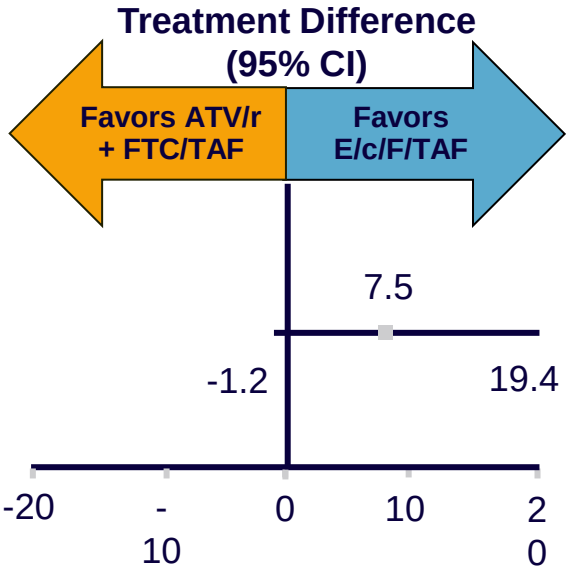
Renal Events Leading to Discontinuation, n	TAF (n = 866)	TDF (n = 867)
Proximal renal tubulopathy	0	4
Cr elevation or eGFR decrease	0	3
Renal failure	0	2
Nephropathy	0	1
Proteinuria	0	1
Bladder spasm	0	1
Total	**0**	**12**

Arribas JR, et al. CROI 2017. Abstract 453.

WAVES:
Switch to E/C/F/TAF in Women at Wk 48

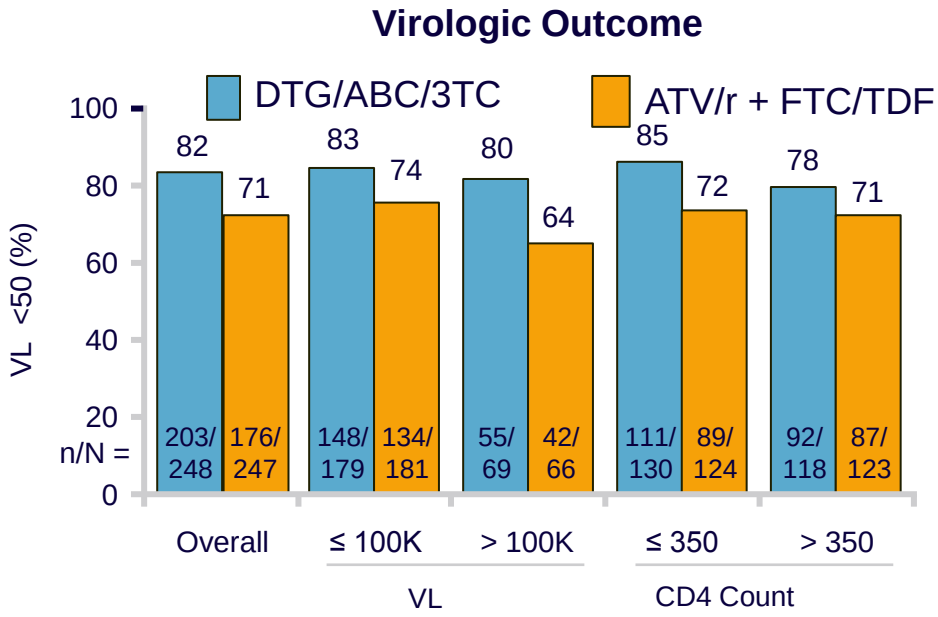
Open-label extension study

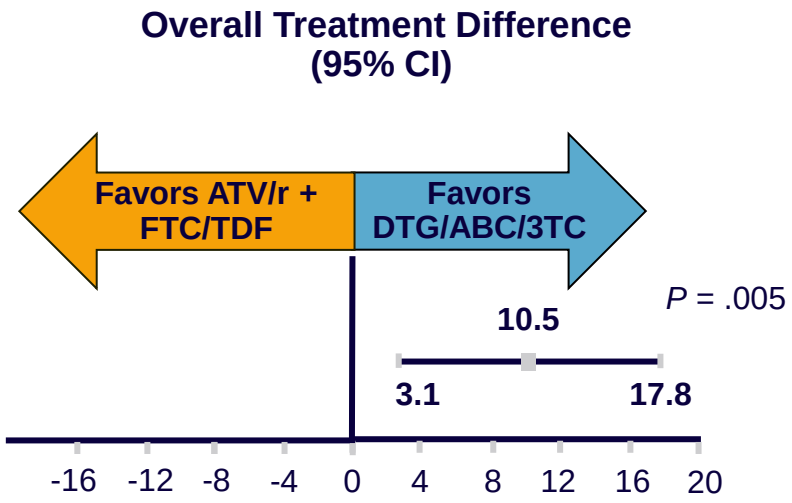




Hodder S, et al. CROI 2017. Abstract 443.

ARIA: DTG/ABC/3TC vs ATV/r + FTC/TDF in ART-Naive Women at Wk 48





Outcome, % (n)	DTG/ABC/3TC (n = 248)	ATV/r + FTC/TDF (n = 247)
Virologic nonresponse	6 (16)	14 (35)
No virologic data	12 (29)	15 (36)

Orrell C, et al. AIDS 2016. Abstract THAB0205LB. Johnson M, et al. HIV Glasgow 2016. Abstract P035. Hagins D, et al. IDWeek 2016. Abstract 949.

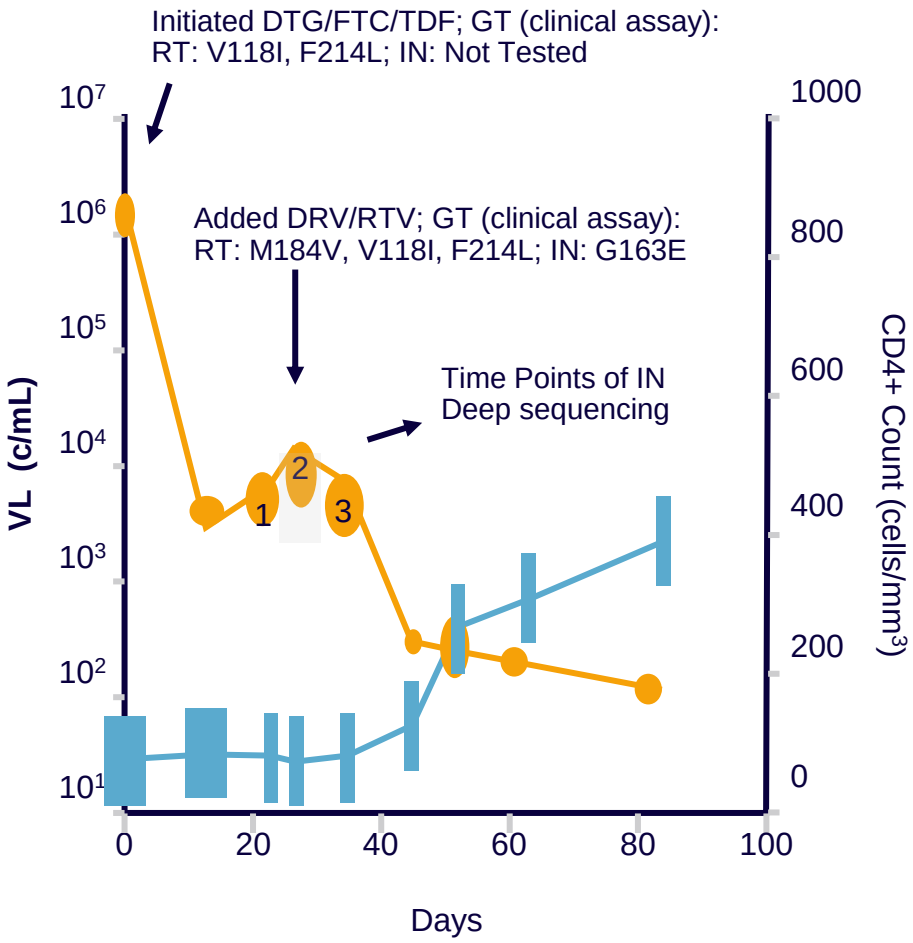
Integrase resistance in the U.S.

- Transmitted INSTI resistance remains rare; rates of on-treatment INSTI resistance remain low[1-3]
- CDC National HIV Surveillance System[1]:
  - Prevalence of INSTI resistance through 2014: 65/14,468 (0.4%)
  - Pre-ART prevalence of INSTI resistance (ie, transmitted): 2/4,631 (0.04%)
- UNC CFAR HIV Clinical Cohort[2]:
  - 2015 INSTI resistance prevalence in 685 pts who began ART in 2007 or later: 1%
- Modeling: assuming 0.1% rate of transmitted INSTI resistance and $250 cost per test: pre-ART INSTI resistance testing correlated with worse outcomes, higher costs vs no test[3]

1. Hernandez AL, et al. CROI 2017. Abstract 478.
2. Davy T, et al. CROI 2017. Abstract 483.
3. Koullias Y, et al. CROI 2017. Abstract 493.

Emergence of INSTI Resistance in Acute Infection Treated With DTG + FTC/TDF

- 45-yo man with PCP and ARS
- Started DTG + FTC/TDF and discharged; readmitted to ICU several days later for hypoxia
- VL increased after readmission despite adherence (including DOT in hospital); no divalent cation use
  - DRV/r added, VL decreased
  - Pneumonia improved; pt discharged
- Rapid INSTI emergence by deep seq: eg, Q148K population increased from 0.0015% at Timepoint 1 to 20.9% at Timepoint 3



Fulcher JA, et al. CROI 2017. Abstract 500LB.

D:A:D: Exposure to ATV/r or DRV/r and Risk of CVD

- Prospective analysis of pts followed from 1/1/09 (BL) to earliest CVD, last visit + 6 mos, or 2/1/16 (N = 35,711)
  - 1,157 (3.2%) developed CVD (MI, CVA, sudden cardiac death, invasive CV procedure)
- Cumulative expos. to DRV/r, but not ATV/r, assoc. with increased CVD risk in multivariate analysis: 59% risk increase per 5-yrs' DRV/r
  - Not mediated by dyslipidemia, in contrast with 1st-generation PIs

CVD Risk per 5 Yrs of ARV Exposure, IRR (95% CI)		
Model	**ATV/r**	**DRV/r**
Univariate	1.25 (1.10-1.43)	1.93 (1.63-2.28)
Multivariate		
▪ Baseline adjusted*	1.03 (0.90-1.18)	1.59 (1.33-1.91)
▪ Time-updated adjusted*	1.01 (0.88-1.16)	1.53 (1.28-1.84)

*Adjusted for: BMI, CKD, DM, CD4, dyslipidemia.

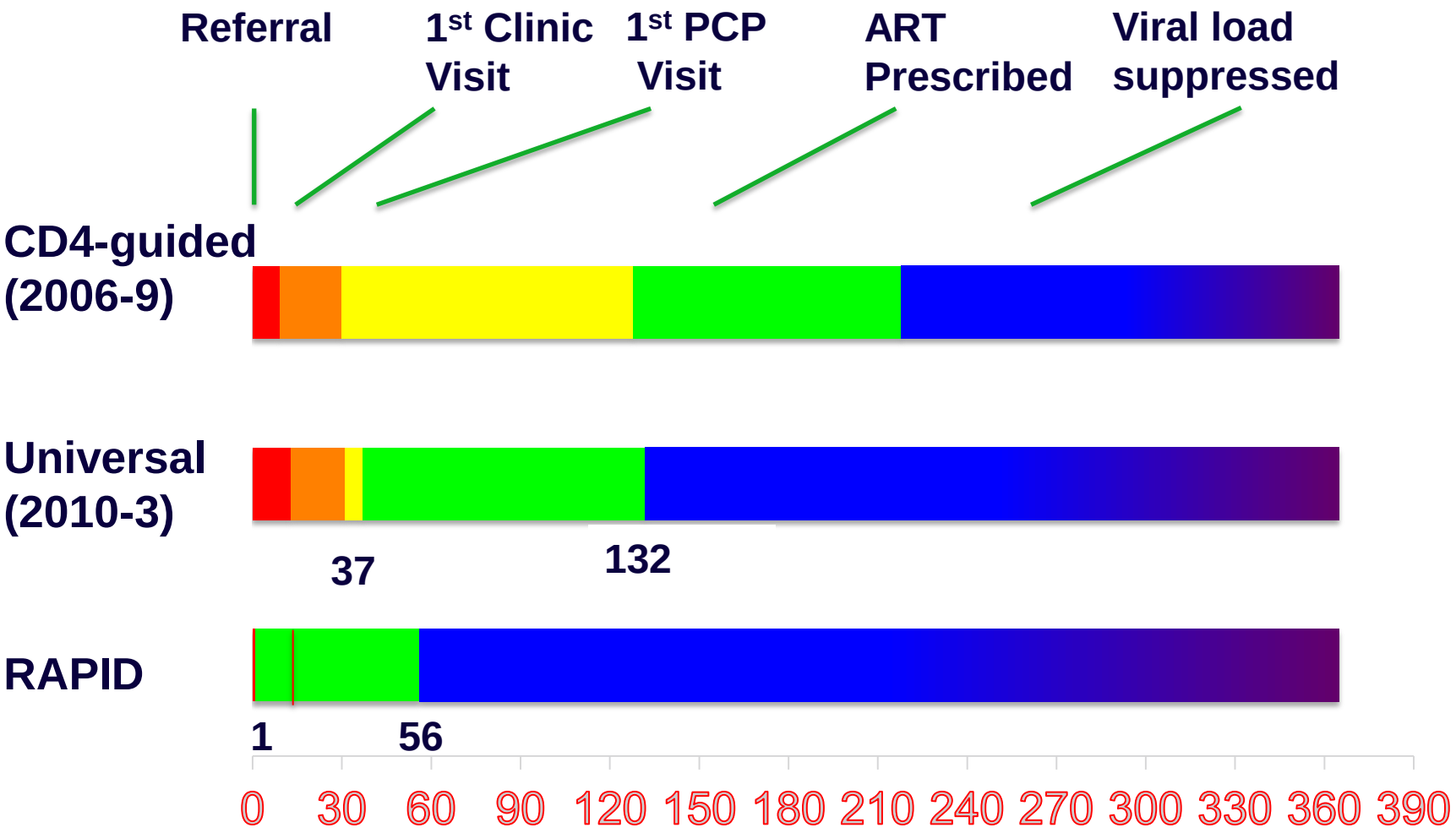
Limitations: potential for unmeasured confounding; observational study; unable to distinguish between DRV/r 800/100 mg QD vs DRV/r 600/100 mg BID; multiple outcomes required

Ryom L, et al. CROI 2017. Abstract 128LB.

Initial Therapy:
My choices for specific clinical scenarios

Scenario	Regimens
Desires single-tablet regimen (STR)	▪ DTG/ABC/3TC ▪ EVG/c/FTC/TAF
STR doesn't matter	▪ DTG + FTC/TAF
HBV Coinfection	▪ FTC/TAF-based regimen
Starting without resistance test results	▪ (DRV/c or DTG) + FTC/TAF
Desire for pregnancy	▪ RAL + (FTC/TDF or ABC/3TC) ▪ DRV/r + (FTC/TDF or ABC/3TC)
Questionable adherence	▪ DTG/ABC/3TC ▪ DRV/c + FTC/TAF
Tuberculosis	▪ EFV/FTC/TDF ▪ RAL 800 mg bid + (FTC/TDF or ABC/3TC)
Drug interactions (including HCV)	▪ DTG or RAL-based regimen

RAPID Start of ART: UCSF experience



Pilcher CD, et al. *J Acquir Immune Defic Syndr* 2016

Rapid Start:
Potential regimens

Regimens to consider

- DTG + FTC/TAF
- EVG/c/FTC/TAF
- DRV/c + FTC/TAF

Drugs to avoid

- ABC (need HLA B*5701)
- TDF (need eGFR)
- RPV (need VL, CD4)
- EFV, NVP (need genotype)

Switching Therapy in Virologically Suppressed Patients

Switching therapy in suppressed patients: When and why?

- To manage side effects
- To manage or prevent drug toxicity
- To simplify regimen (number of doses or pills)
- To address food restrictions
- To address drug interactions
- To plan for pregnancy

Summary of TAF Switch Studies in Virologically Suppressed Patients

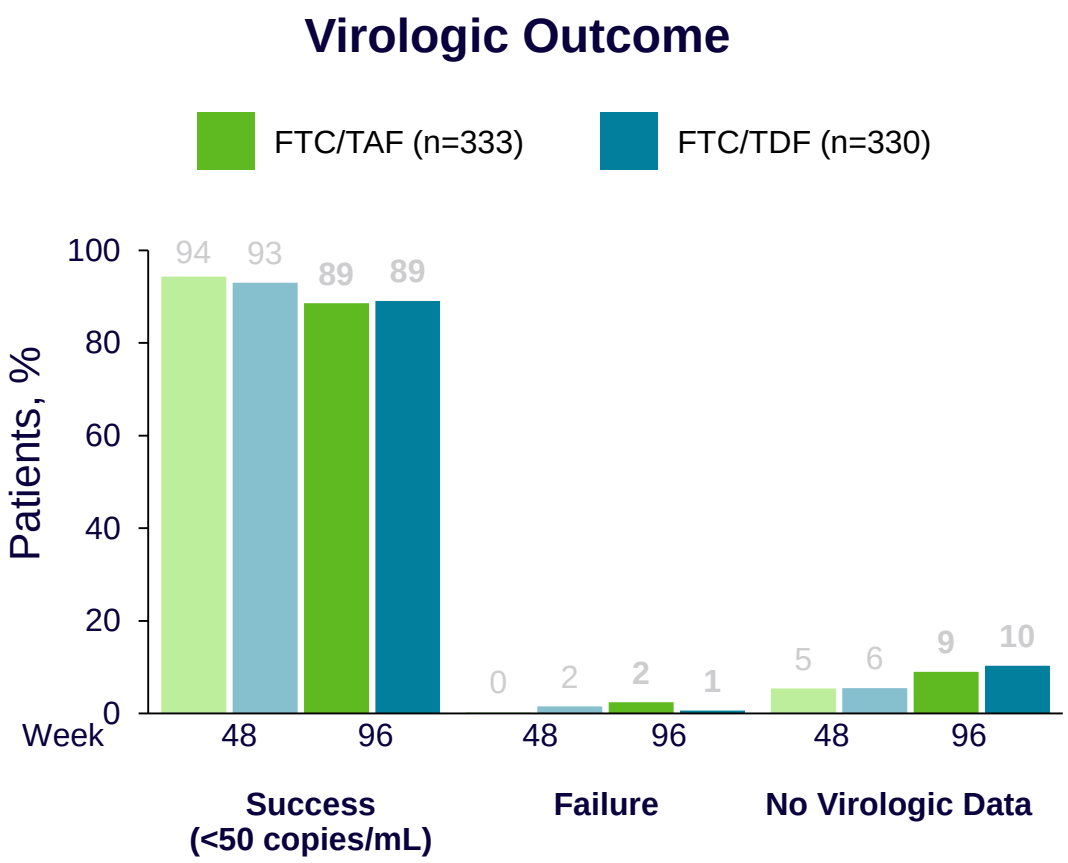
Trials:

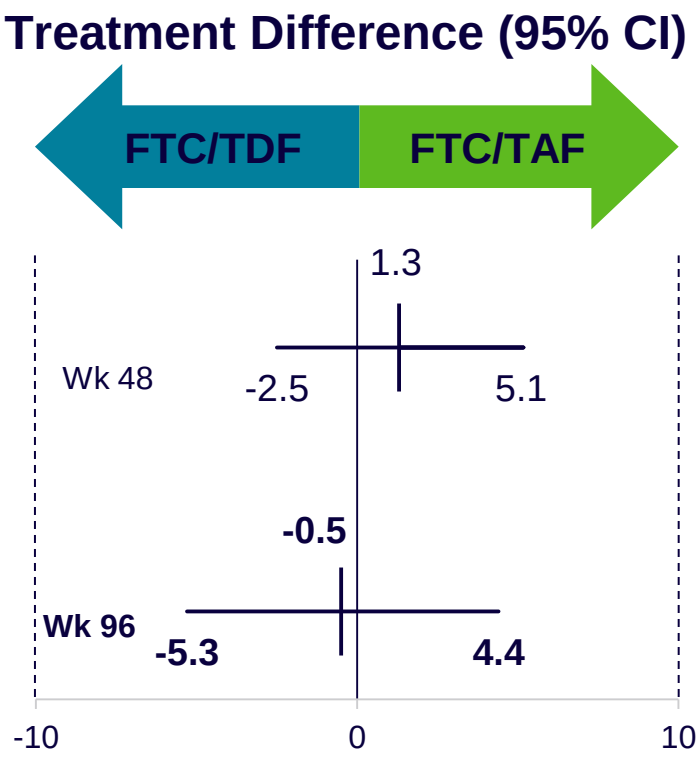
- GS-109: TDF-containing regimens to EVG/COBI/FTC/TAF
- GS -112: Switch to EVG/COBI/FTC/TAF in patients with impaired renal function
- GS-119: ART + DRV/r to EVG/COBI/FTC/TAF + DRV in ART-experienced patients
- GS-1089: FTC/TDF to FTC/TAF
- GS-1160: EFV/FTC/TDF to RPV/FTC/TAF
- GS-1216: RPV/FTC/TDF to RPV/FTC/TAF

Results:

- Noninferiority, with superiority in GS-109 (switch from EFV/FTC/TDF or ATV/r + FTC/TDF) and superiority in GS-119
- Increase in bone density
- Stability of eGFR (increase in GS-1089 and GS-112) with no tubular toxicity and decrease in overall and tubular proteinuria

GS 1089: Switch from F/TDF to F/TAF Weeks 48 and 96 Efficacy

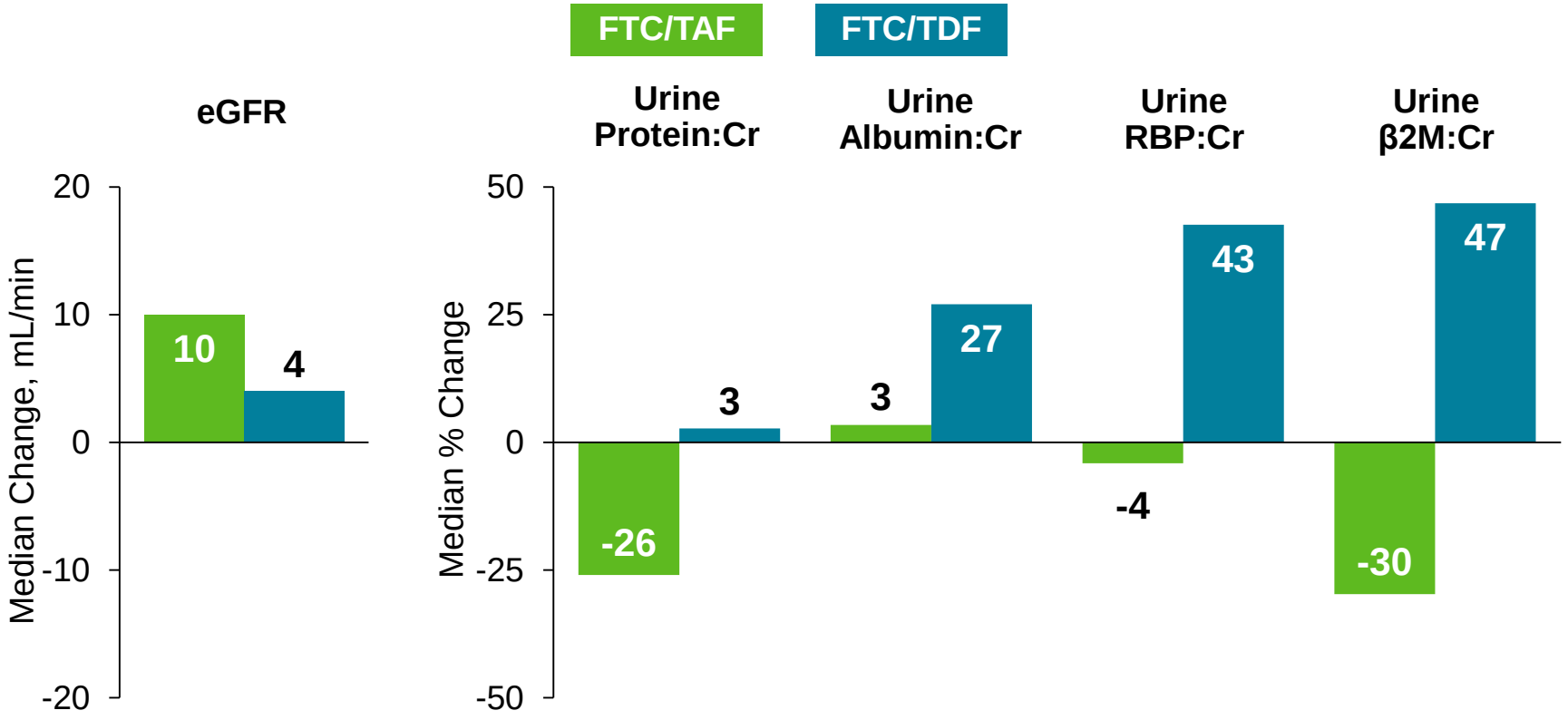




FTC/TAF noninferior to FTC/TDF at Weeks 48 and 96

Raffi F, et al. HIV Glasgow, October 2016, Glasgow, UK, Presentation O125

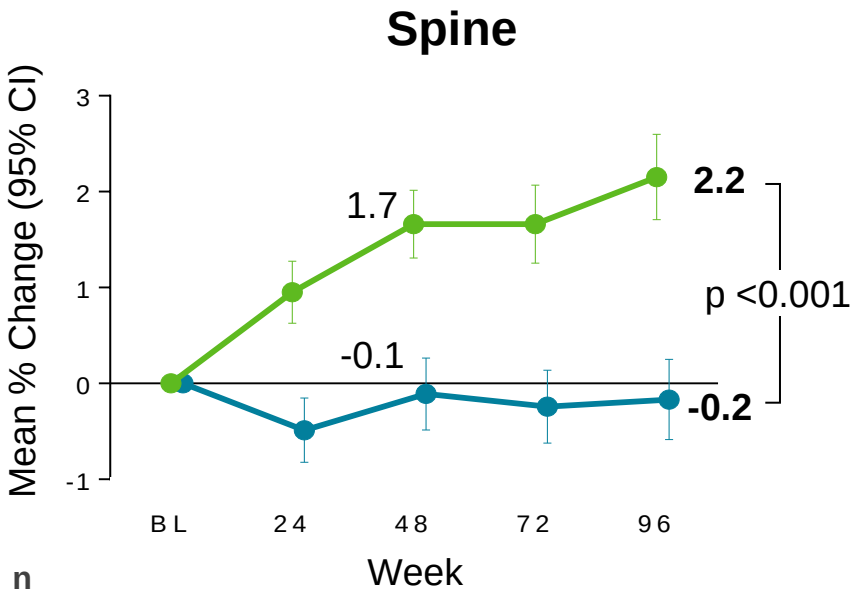
GS 1089: Switch from F/TDF to F/TAF
Change in Renal Biomarkers at Weeks 48 and 96

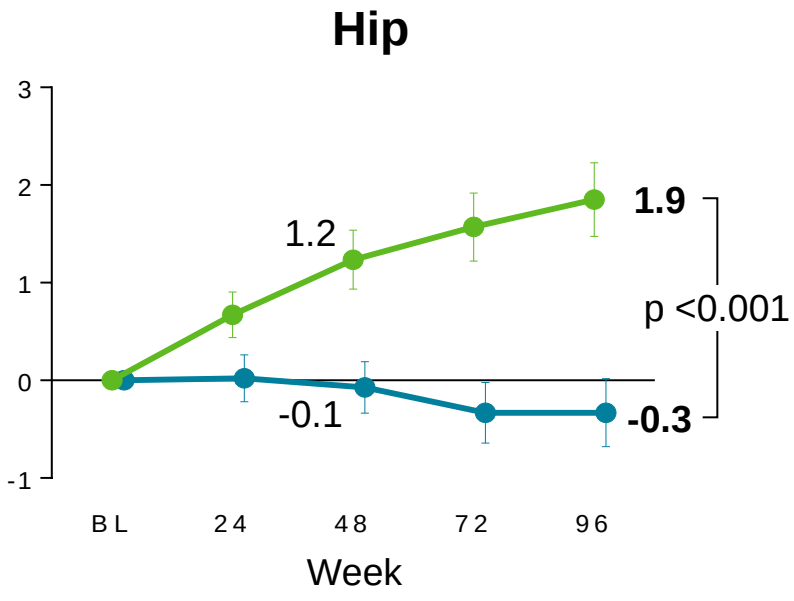


All differences between treatments statistically significant (p <0.001)

Raffi F, et al. HIV Glasgow, October 2016, Glasgow, UK, Presentation O125

GS 1089: Switch from F/TDF to F/TAF: Bone density changes through Week 96





n					
FTC/TAF	321	310	300	294	287
FTC/TDF	320	310	306	297	292

n					
FTC/TAF	321	309	300	293	288
FTC/TDF	317	305	303	296	289

	FTC/TAF	FTC/TDF	p value
≥3% increase	40%	18%	< 0.001
≥3% decrease	8%	19%	< 0.001

	FTC/TAF	FTC/TDF	p value
29%	11%	< 0.001	
6%	15%	< 0.001	

Raffi F, et al. HIV Glasgow, October 2016, Glasgow, UK, Presentation O125

TDF to TAF switch

Advantages:

- Increased eGFR
- Decreased proteinuria
- Improved bone density
- Smaller pill size

Disadvantages:

- Loss of TDF lipid effect
- TAF will be more expensive than *generic* TDF

IAS-USA recommendations: “If there is no increase in the price of TAF vs. that of TDF, switching from TDF to TAF is reasonable even if patients are not experiencing TDF-related toxic effects.”

Günthard HF, et al. *JAMA* 2016;316:191-210.

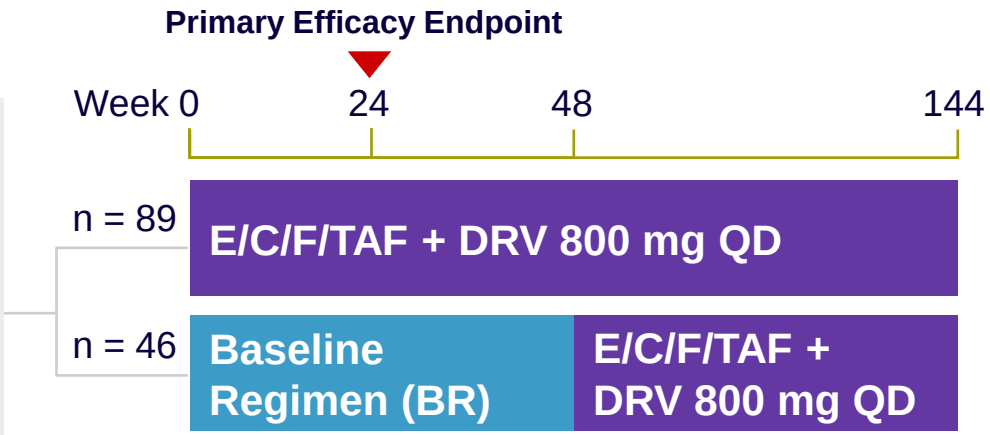
Switch Studies in Virologically Suppressed Pts

Trial	From	To	Outcome vs Suppressive ART
GS-123[1]	TDF/FTC + RAL	E/C/F/TDF	Virologic suppression maintained
GS-264[2]	TDF/FTC/EFV	RPV/FTC/TDF	Virologic suppression maintained
Strategy-NNRTI[3]	TDF/FTC + NNRTI	E/C/FTC/TDF	Noninferior or superior
Strategy-PI[4]	TDF/FTC + PI/r	E/C/F/TDF	Noninferior or superior
SPIRIT[5]	2 NRTI + PI/r	RPV/FTC/TDF	Noninferior or superior
SPIRAL[6]	2 NRTI + PI/r (exp'd pts)	RAL + 2 NRTI	Noninferior or superior
SALT[7]	ATV/r + 2 NRTI	ATV/r + 3TC	Noninferior or superior
OLE[8]	LPV/r + 2 NRTIs	LPV/r + 3TC	Noninferior or superior
GS-109[9]	TDF-based ART	E/C/F/TAF	Noninferior or superior
STRIIVING[10]	Suppressive ART	DTG/ABC/3TC	Noninferior or superior
ATLAS-M[11]	ATV/r + 2 NRTIs	ATV/r + 3TC	Noninferior or superior
GS-119[12]	DRV/r-containing "salvage" regimen	E/C/F/TAF + DRV	Noninferior or superior
LATTE[13]	CAB or EFV + 2 NRTIs	CAB + RPV (PO)	Noninferior or superior
GS-1089[14]	TDF/FTC + 3rd agent	TAF/FTC + 3rd agent	Noninferior or superior
LATTE-1[15 – TBD]	CAB + ABC/3TC	CAB + RPV (IM)	Noninferior or superior
GS-1160[16]	EFV/FTC/TDF	RPV/FTC/TAF	Noninferior or superior
GS-1216[16]	RPV/FTC/TDF	RPV/FTC/TAF	Noninferior or superior
SWORD-1 & 2[17]	3-drug regimen	DTG + RPV	Noninferior or superior

GS 119: E/C/F/TAF + DRV for treatment-experienced patients

Randomized (2:1), open-label (N = 135)

Eligibility:
- ≥4 mos <50 on ART containing DRV
- 2 prior failures ≥2-class resistance by historical genotype (inc. ≤3 TAMs and K65R)
- Historical genotype with no INSTI-R or currently on RAL
- No Q151M, T69ins, or DRV RAMS
- eGFR >50 mL/min



Objectives
- Primary
  - Efficacy of E/C/F/TAF + DRV vs BR at Week 24: FDA snapshot (<50)
- Secondary
  - Safety and tolerability in both treatment arms over 24 and 48 weeks
  - Efficacy at Week 48: VL <50
  - Efficacy at Week 48: VL <20

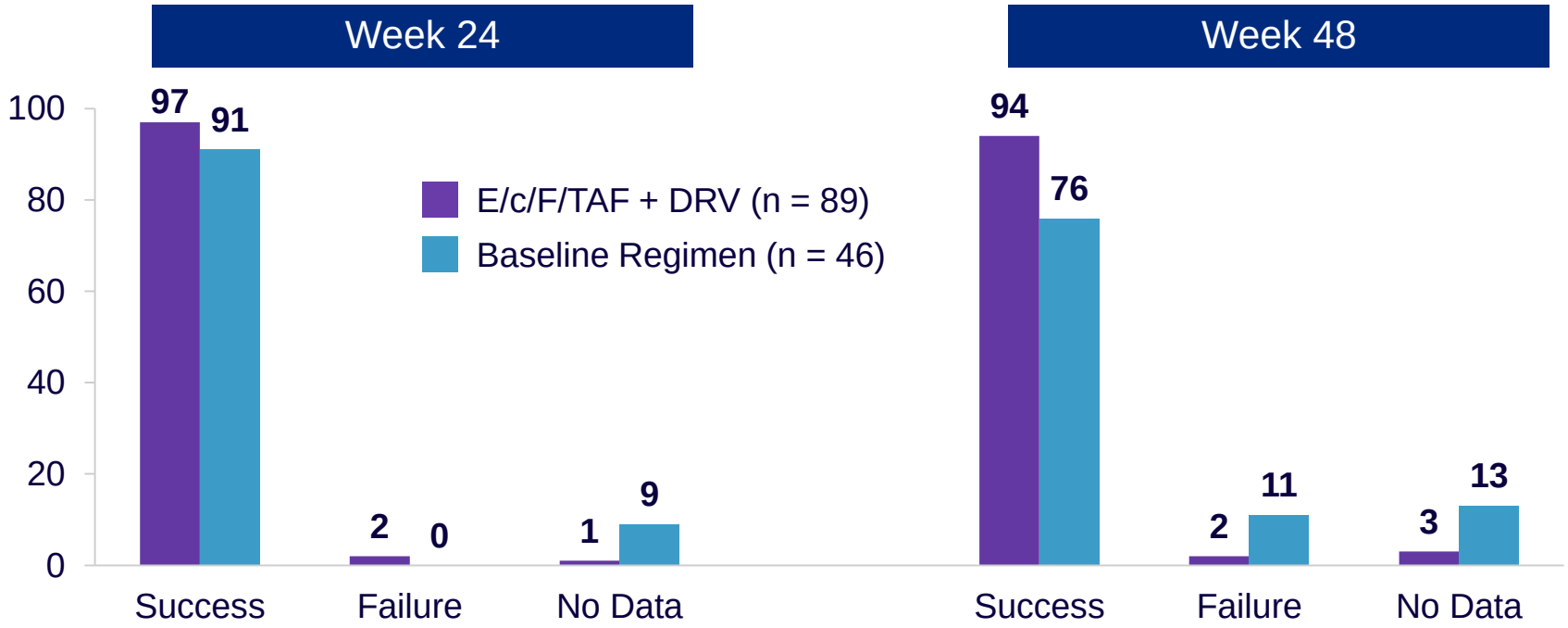
Huhn G, et al. *J Aquir Immune Defic Syndr* 2016;74:193-200.

GS 119: Baseline Characteristics

%, unless otherwise indicated **Characteristics**	**E/C/F/TAF + DRV n = 89**	**Baseline Regimen n = 46**
Median age, years	49	47
Male	82	61
Black (or African descent)	39	57
Median CD4 count, cells/μL	519	518
Median $eGFR_{CG}$, mL/min	99	100
DM / HTN / CVD / Hyperlipidemia	8 / 34 / 7 / 46	11 / 37 / 4 / 28
Baseline Regimen		
Median no. pills per day	5	5
≥6 pills per day	40	37
At least BID dosing	65	65
TDF / ABC / other NRTIs	61 / 11 / 12	54 / 11 / 13
RAL	56	50
Resistance		
2-class / 3-class resistance	70 / 26	74 / 20
M184V/I	85	78
K65R	20	30
NNRTI-R / PI-R	89/ 38	87 / 28

Huhn G, et al. *J Aquir Immune Defic Syndr* 2016;74:193-200.

GS 119: Virologic Outcome (VL<50) Weeks 24 and 48

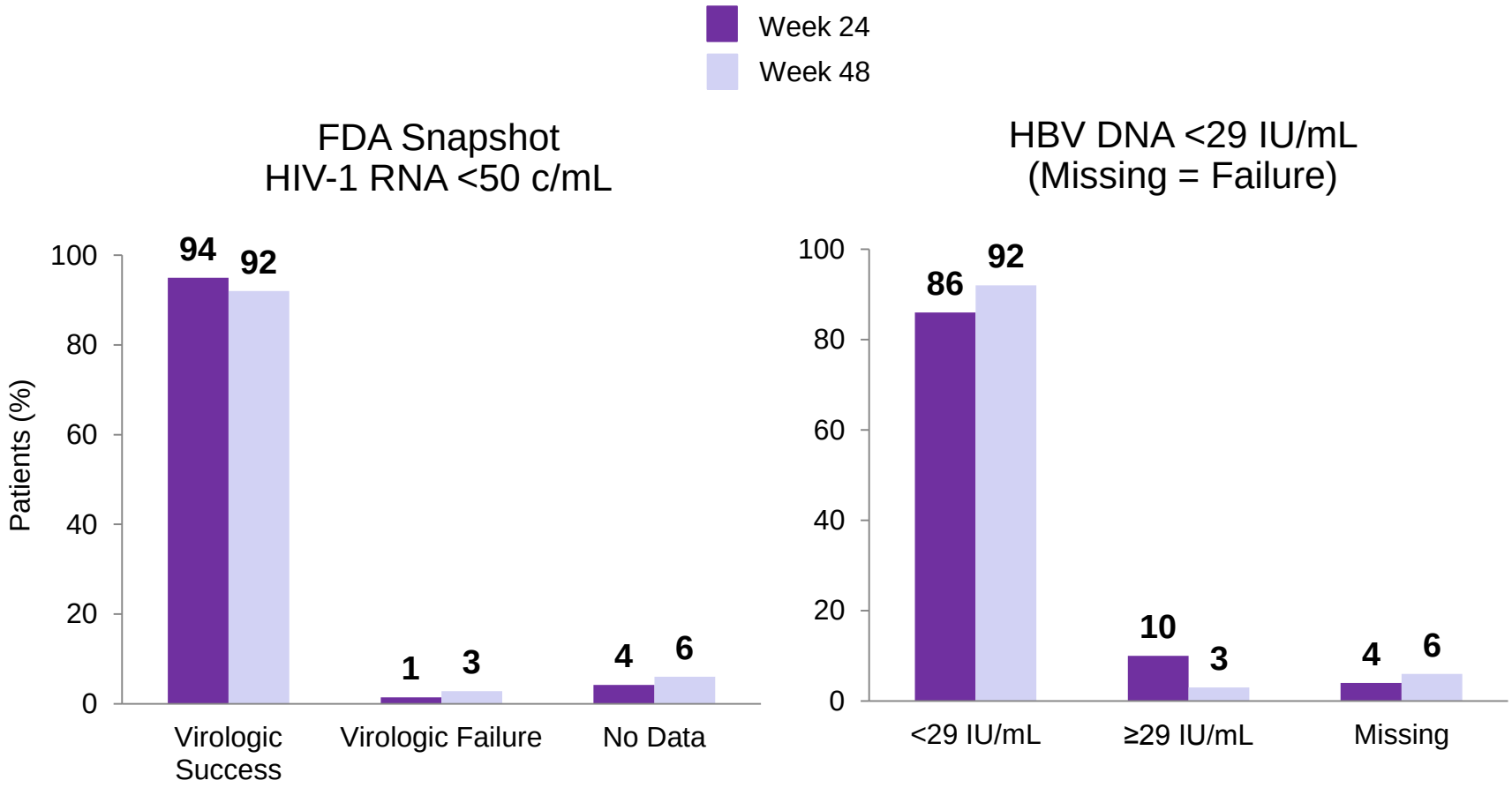


Proportional difference (95% CI)	5.3% (-3.4%, 17.4%) p = 0.23	18.3% (3.5%, 33.0%) p = 0.004

- At Week 48, higher virologic success (VL <20) with E/c/F/TAF + DRV vs BR (90% vs 72%, p = 0.012)
- No emergent resistance in E/c/F/TAF + DRV arm; 1 pt with viral rebound (Week 36) developed resistance (M184V+K65R) in BR arm

Huhn G, et al. *J Aquir Immune Defic Syndr* 2016;74:193-200.

GS-1249: Switch to E/c/F/TAF in HIV/HBV coinfected patients



Outcomes of 3 patients on non-TDF-based regimens

- LPV/r+ ABC/3TC: HIV RNA <50 c/mL; HBV DNA declined from 143 to <20 IU/mL
- RAL+ATV/r : HIV RNA remained <50 c/mL; HBV DNA declined from 259,000,000 to 51 IU/mL
- ATV/r monotherapy: HIV RNA remained <50 c/mL; HBV DNA remained <20 IU/mL

Gallant J, et al. *JAIDS* 2016;73:294-298.

Switch Studies in Virologically Suppressed Pts

Trial	From	To	Outcome vs Suppressive ART
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GS-264[2]	TDF/FTC/EFV	RPV/FTC/TDF	Virologic suppression maintained
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Strategy-PI[4]	TDF/FTC + PI/r	E/C/F/TDF	Noninferior or superior
SPIRIT[5]	2 NRTI + PI/r	RPV/FTC/TDF	Noninferior or superior
SPIRAL[6]	2 NRTI + PI/r (exp'd pts)	RAL + 2 NRTI	Noninferior or superior
SWITCHMRK[18]	2 NRTI + LPV/r (exp'd pts)	2 NRTI + RAL	✗
HARNESS[19]	2 NRTI + 3rd Agent	ATV/r + RAL	✗
STRIIVING[10]	Suppressive ART	DTG/ABC/3TC	Noninferior or superior
ATLAS-M[11]	ATV/r + 2 NRTIs	ATV/r + 3TC	Noninferior or superior
GS-119[12]	DRV/r-containing "salvage" regimen	E/C/F/TAF + DRV	Noninferior or superior
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GS-1160[16]	EFV/FTC/TDF	RPV/FTC/TAF	Noninferior or superior
GS-1216[16]	RPV/FTC/TDF	RPV/FTC/TAF	Noninferior or superior
SWORD-1 & 2[17]	3-drug regimen	DTG + RPV	Noninferior or superior

SWITCHMRK: Prior failure predicts failure

Inferior efficacy of RAL appeared driven by more failure among pts with previous virologic failure

Outcome	SWITCHMRK1		SWITCHMRK 2	
	RAL (n = 174)	LPV/r (n = 174)	RAL (n = 176)	LPV/r (n = 178)
Patients *without* previous virologic failure				
▪ VL <50 at Wk 24, %	85.1	85.8	92.5	93.5
▪ Treatment difference, % (95% CI)	-0.7 (-9.9 to 8.6)		-1.0 (-8.5 to 6.3)	
Patients *with* previous virologic failure				
▪ VL <50 at Wk 24, %	72.3	89.7	79.7	93.8
▪ Treatment difference, % (95% CI)	**-17.3 (-33.0 to -2.5)**		**-14.2 (-26.5 to -2.6)**	

Eron JJ, et al. *Lancet*. 2010;375:396-407.

Switching: Caveats

- Know the treatment and resistance history
- Avoid switching from high-barrier to lower-barrier agents when you don’t know history
- Consider archive DNA genotype when you can’t get old records

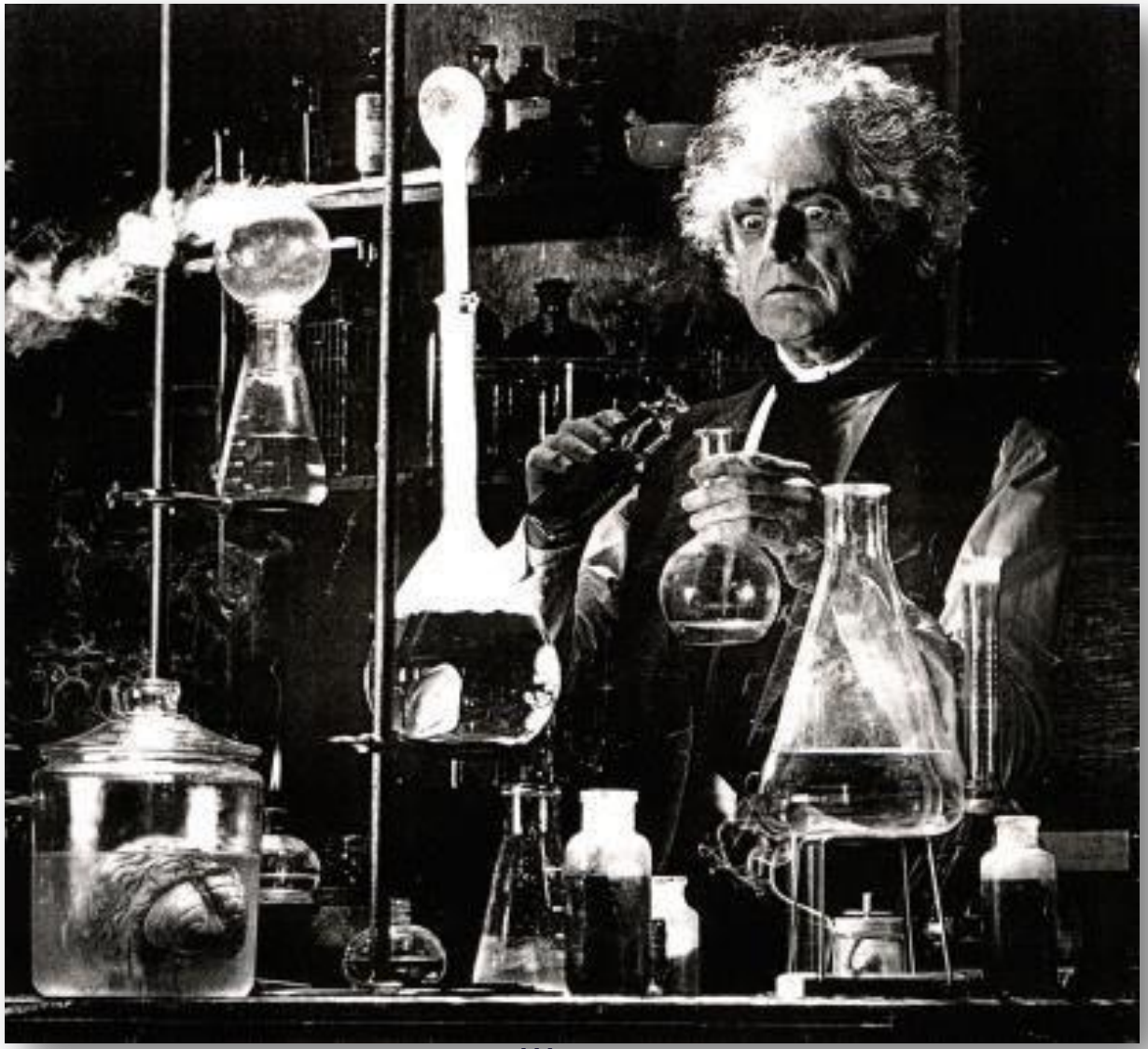
Concordance of archived DNA Assay with historical resistance profile

Separate studies evaluated concordance of resistance mutation profile in HIV DNA identified with archive assay vs patient's historical resistance profile

Resistance in Assay vs Historical Genotype, %	Study 1[1] (N = 48)	Study 2[2] (N = 140)
Concordance	85	91
• NNRTIs	93	73
• PIs	84	77
• NRTIs	76	73
False omission	3	12

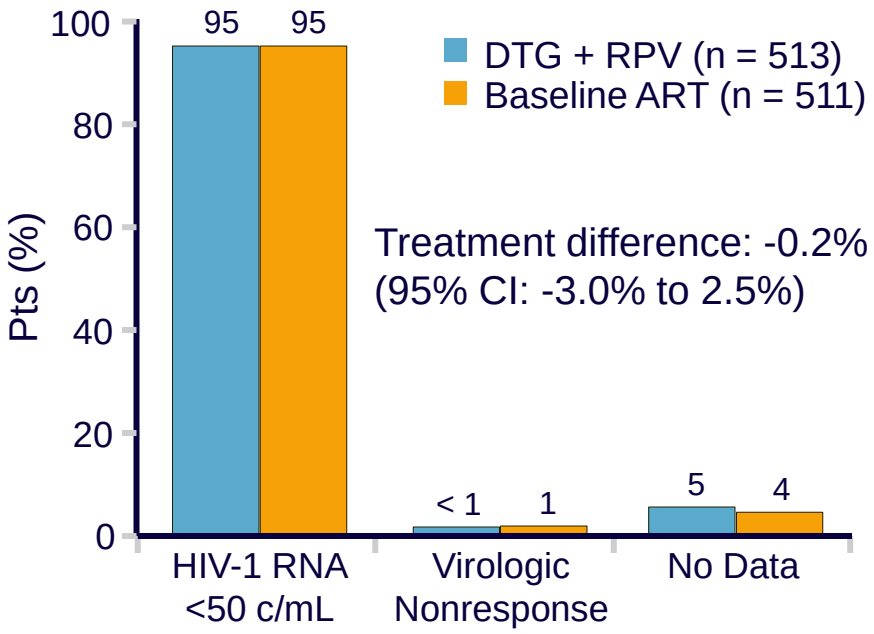
1. Toma J, et al. ICAAC 2015. Abstract 1662.
2. Singh H, et al. Open Forum Infect Dis. 2016;3:1507.

Investigational Strategies



…using approved drugs

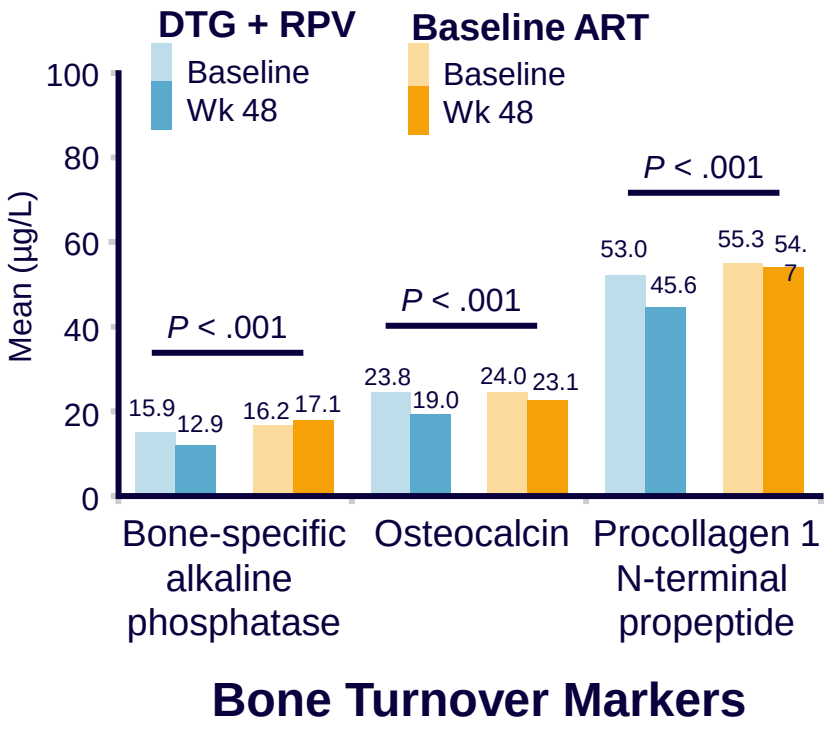
SWORD 1 & 2: Switch From Suppressive ART to DTG + RPV



- Open-label, multicenter phase III trials of pts with virologic suppression (N = 1024) randomized to continue baseline ART vs switch to DTG + RPV
- 1 pt with confirmed criteria for virologic withdrawal at Wk 36 in DTG + RPV arm had K101K/E
  - Documented nonadherence at VF
  - Resuppressed with continued DTG + RPV
  - No INSTI resistance

Llibre JM, et al. CROI 2017. Abstract 44LB.

SWORD 1 & 2: Switch from Suppressive ART to DTG + RPV: Safety Outcomes



Bone Turnover Markers

- AE rates generally similar between arms through Wk 52
  - Numerically higher rate of drug-related grade 1/2 AEs with switch: 17% vs 2%
  - Numerically higher rate of withdrawal for AEs with switch: 4% vs <1%
- No notable change in lipids through Wk 48 in either treatment arm

Llibre JM, et al. CROI 2017. Abstract 44LB.

PADDLE: Dolutegravir + Lamivudine for Treatment-Naive Pts

	HIV-1 RNA (copies/mL)														
Pt #	Screen	BL	Day 2	Day 4	Day 7	Day 10	Wk 2	Wk 3	Wk 4	Wk 6	Wk 8	Wk 12	Wk 24	Wk 36	Wk 48
1	5584	10,909	3701	383	101	71	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
2	8887	10,233	5671	318	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
3	67,335	**151,569**	37,604	1565	1178	266	97	53	< 50	< 50	< 50	< 50	< 50	< 50	< 50
4	99,291	**148,370**	11,797	3303	432	179	178	55	< 50	< 50	< 50	< 50	< 50	< 50	< 50
5	34,362	20,544	4680	1292	570	168	107	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
6	16,024	14,499	3754	1634	162	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
7	37,604	18,597	2948	819	61	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
8	25,071	24,368	6264	1377	Not done	268	105	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
9	14,707	10,832	Not done	516	202	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	SAE	
10	10,679	7978	5671	318	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
11	50,089	**273,676**	160,974	68,129	3880	2247	784	290	288	147	< 50	< 50	< 50	< 50	< 50
12	13,508	64,103	3496	3296	135	351	351	84	67	< 50	< 50	< 50	< 50	< 50	< 50
13	28,093	33,829	37,350	26,343	539	268	61	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
14	15,348	15,151	3994	791	198	98	< 50	61	64	< 50	< 50	< 50	< 50	< 50	< 50
15	23,185	23,500	15,830	4217	192	69	< 50	< 50	< 50	Not done	< 50	< 50	< 50	< 50	< 50
16	11,377	3910	370	97	143	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
17	39,100	25,828	11,879	1970	460	147	52	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
18	60,771	73,069	31,170	2174	692	358	156	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
19	82,803	**106,320**	35,517	2902	897	352	168	76	< 50	< 50	< 50	< 50	< 50	Virologic failure	
20	5190	7368	3433	147	56	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50

Cahn P, et al. AIDS 2016. Abstract FRAB0104LB.

ANRS 167 LAMIDOL:
Switch to DTG + 3TC in Suppressed Pts

Noncomparative, open-label, single-arm multicenter trial

1º endpoint: therapeutic success at Wk 56 (ie, after 48 wks of dual therapy)

Therapeutic failure: VL >50 interruption, lost to f/u, death

*Pts with VL ≤50 proceeded to phase II.
†In phase I, third agent in regimen replaced with DTG; baseline NRTI backbone maintained.

Joly V, et al. CROI 2017. Abstract 458.

ANRS 167 LAMIDOL: Switch to DTG + 3TC in Suppressed Pts

- 97% (101/104) remained suppressed through 40 wks of dual therapy (study Wk 48)[1]
  - No INSTI resistance in 3 pts with virologic failure
  - 7 with SAEs, only 2 related to dual therapy
- Switch to DTG-based dual therapy vs continued triple ART currently under evaluation in several phase III trials[2,3]

Therapeutic Success, n/N* (%)	DTG + 3TC
Wk 0 (entry; on BL triple therapy)	110/110 (100)
Wk 8 (end of phase I, start of phase II)	104/104 (100)
Wk 12	104/104 (100)
Wk 16	103/104 (99)
Wk 24	103/104 (99)
Wk 32	103/104 (99)
Wk 40	102/104 (98)
Wk 48	101/104 (97)

*Pts enrolled in phase I, N = 110; pts enrolled in phase II, N = 104.

1. **Joly V, et al. CROI 2017. Abstract 458.**
2. **ClinicalTrials.gov. NCT02263326.**
3. **ClinicalTrials.gov. NCT02486133.**

DOMOMO: Switch to DTG Monotherapy in Suppressed Pts

- Randomized comparison: switch to DTG monotherapy vs continued baseline ART for 24 wks in suppressed pts without previous VF[2]
- At Wk 24, DTG monotherapy noninferior to continued baseline ART (VL <200)
  - After 24 wks, all pts allowed to switch to monotherapy
- Study stopped early because of high VF rate after 48 wks of monotherapy
  - VF in 8/77 pts with DTG monotherapy vs 3/152 pts on combination ART in concurrent control group (*P* = .03)
  - Among 6 VF cases with resistance data in DTG monotherapy group, 3 developed INSTI resistance

Wijting I, et al. CROI 2017. Abstract 451LB.

Emergent INSTI Resistance after Switch to DTG Monotherapy

- International, multicenter retrospective study
  - Evaluated virologically suppressed pts switched to DTG monotherapy
  - Pts with history of VF on INSTI and INSTI resistance excluded
- 11 of 122 pts (9%) switched to DTG monotherapy experienced VF
  - 9 of 11 had genotypic INSTI resistance at VF

INSTI resistance pathways varied

INSTI Resistance at VF
92Q/155H (n = 1)
97A/155H (n = 1)
155H/148R (n = 1)
118R (n = 2)
148K (n = 1)
148H (n = 2)
148R (n = 1)

Blanco JL, et al. CROI 2017. Abstract 42.

Conclusions

- INSTI-based regimens are now the standard of care for initial therapy
- TAF/FTC is the preferred NRTI backbone for all regimens except DTG/ABC/3TC
- Some regimens allow for immediate ART initiation while awaiting baseline lab results
- Switching from TDF to TAF increases bone density and eGFR and decreases proteinuria
- In experienced patients, consider prior resistance and new resistance barrier before switching therapy
- Stay tuned for The Great Debate: 3 drugs vs 2
- DTG resistance can happen but is *rare…*
- *…*except with DTG monotherapy. *Don't do it!*

HIV Management
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