

ARV Therapies and Therapeutic Strategies
INDEPENDENT REPORTING ON EACS 2017

COMPREHENSIVE EXPERT REVIEW
AND DISCUSSION OF KEY PRESENTATIONS

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**RANDOMIZED DOUBLE-BLIND TRIAL COMPARING SWITCHING
TO FTC/TAF- VERSUS CONTINUING ABC/3TC-BASED REGIMENS
IN VIROLOGICALLY SUPPRESSED ADULTS (STUDY 1717):
48 WEEK RESULTS**

Alan Winston, Frank A. Post, Edwin DeJesus, Daniel Podzamczar,
Giovanni Di Perri, Vicente Estrada, François Raffi, Peter Ruane,
Patrick Mallon, Francesco Castelli, Mingjin Yan, Stephanie Cox,
Moupali Das, Andrew Cheng, Martin S. Rhee

Abstract PS8/4

BACKGROUND

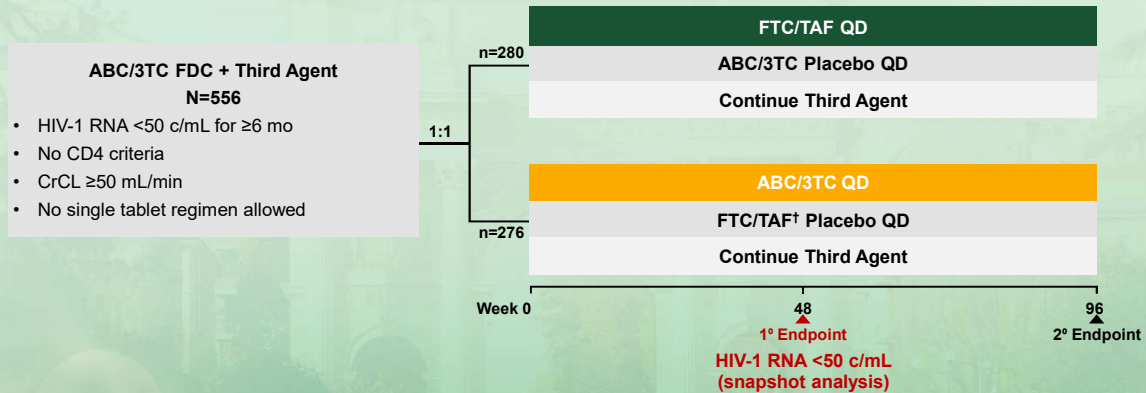
All recommended regimens contain one of the following N(t)RTI agents¹⁻³

- Tenofovir disoproxil fumarate (TDF)
 - Associated with decline in renal function and bone mineral density (BMD)
- Abacavir (ABC)
 - No renal or bone toxicities
 - Associated with cardiovascular risk in some observational and randomized studies
 - In persons with high viral load, concerns exist using some ABC-containing regimens
- Tenofovir alafenamide (TAF)
 - Switch from TDF to TAF leads to improvement in renal function and BMD¹, whilst maintaining virologic suppression⁴
- To date, no head-to-head comparison of emtricitabine plus TAF (FTC/TAF) to ABC plus lamivudine (ABC/3TC)

1. Günthard HF, et al. JAMA 2016;
2. <https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-treatment-guidelines/0/>;
3. http://www.eacsociety.org/files/guidelines_8.2-english.pdf;
4. Gallant JE, et al. Lancet HIV 2016.

GS1717 STUDY: ABC/3TC TO FTC/TAF IN SUPPRESSED INDIVIDUALS

Phase 3, Randomized, Double-blind, Double-dummy,
Active-controlled Study in US and EU



Winston A, et al. 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS84.

GS1717 STUDY: BASELINE CHARACTERISTICS

	FTC/TAF n=280	ABC/3TC n=276
Age, y (range)	52 (20, 79)	52 (24, 74)
Female	40 (14)	61 (22)
Race		
White	205 (73)	199 (72)
Black or African descent	64 (23)	66 (24)
Other	11 (4)	11 (4)
CD4 count, cells/mm ³	654 (489, 849)	700 (546, 891)
CrCL*, mL/min	100 (83, 118)	101 (82, 123)
Duration on ABC/3TC, y	8 (3, 11)	8 (4, 11)
Hyperlipidemia	131 (47)	140 (51)
Hypertension	109 (39)	111 (40)
Diabetes	33 (12)	36 (13)
Cardiovascular disease	18 (6)	16 (6)

Data are median (IQR) or n (%), unless specified otherwise;
 *CrCL calculated with Cockcroft-Gault equation.

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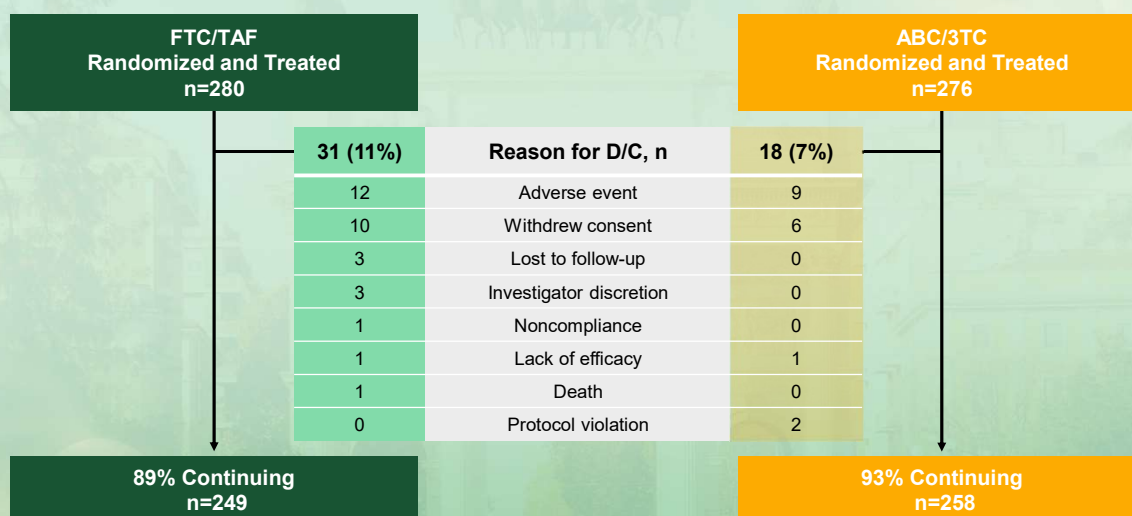
GS1717 STUDY: USE OF THIRD AGENT AT BASELINE

Third Agent, %	FTC/TAF n=280	ABC/3TC n=276
NNRTI	51	53
NVP	29	27
EFV	16	18
RPV	6	8
Boosted PI	30	30
DRV	18	18
ATV	11	9
LPV	1	3
INSTI	19	16
RAL	12	12
DTG*	6	4
Other	1	<1

* Single tablet regimen ABC/3TC/DTG was not allowed.

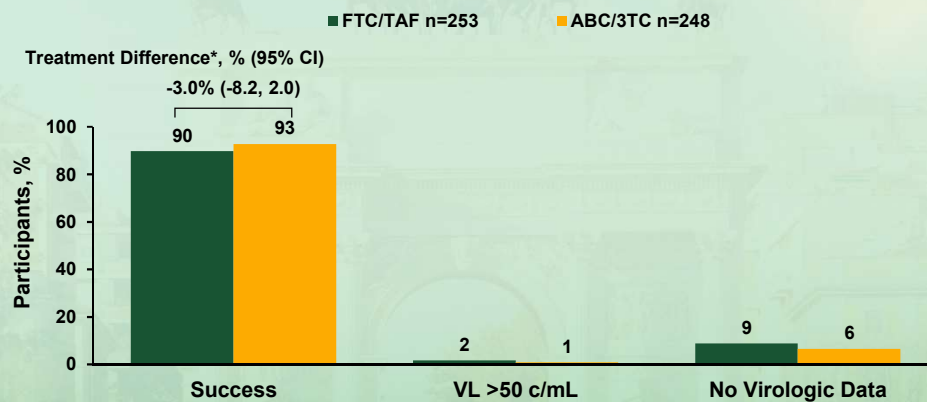
Winston A, et al. 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS84.

GS1717 STUDY: PATIENT DISPOSITION THROUGH WEEK 48



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GS1717 STUDY: EFFICACY AT WEEK 48 (SNAPSHOT)



- Per protocol analysis[†]: 99.1% vs 99.1% (Diff: 0.0% [95% CI: -2.5 to 2.3])

* Non-inferiority margin -10%.

† Excluding major protocol violations, discontinuations for reasons other than lack of efficacy, or nonadherence (<2.5 percentile).

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GS1717 STUDY: TREATMENT EMERGENT RESISTANCE

n (%)	FTC/TAF n=253	ABC/3TC n=248
Analyzed for emergent resistance*	4 (1.6)	1 (0.4)
Development of emergent resistance	1 (0.4)	1 (0.4)
NRTI: K65K/R	1	0
PI: M46I + I50L + N88S	0	1

*Confirmed HIV-1 RNA ≥ 50 c/mL at any visit or unconfirmed >400 c/mL at endpoint or discontinuation.

Winston A, et al. 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS84.

GS1717 STUDY: ADVERSE EVENTS

All Grades ≥5% in Either Group, %	FTC/TAF n=280	ABC/3TC n=276
Nasopharyngitis	13	11
Upper respiratory tract infection	9	12
Diarrhea	9	9
Headache	7	5
Arthralgia	6	7
Cough	6	5
Fatigue	5	4
Back pain	5	6
Urinary tract infection	2	5

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GS1717 STUDY: ADVERSE EVENTS LEADING TO DISCONTINUATION

FTC/TAF (n=280)	ABC/3TC (n=276)
12 (4%)	9 (3%)
Abdominal distension* / myalgia*	Affective disorder*
Anxiety*	Depression* / bone pain* / arthralgia*
Brugada syndrome (asymptomatic)*†	Depression / suicide attempt
Cough	Dermatitis* / pruritus*
Increased blood creatinine*	Diarrhea*
Lymph node tuberculosis	Myalgia* / dysesthesia*
Nausea* / feeling jittery* / decreased appetite*	Panic attack*
Nausea* / vomiting* / dehydration* / acute kidney injury	Rash* / pruritus*
Neutropenia (later diagnosed with acute myeloid leukemia)	Tinnitus* / dry mouth* / dyspnea*
Sudden cardiac death	
Toothache / burning sensation* / headache* / paresthesia*	
Vision blurred* / visual field defect* / eye pain*	

■ No reported cases of proximal renal tubulopathy or Fanconi syndrome in either group

* Considered related to study drug by the investigator.
† Genetically inherited condition, characterized by abnormal ECG findings and an increased risk of sudden cardiac death.

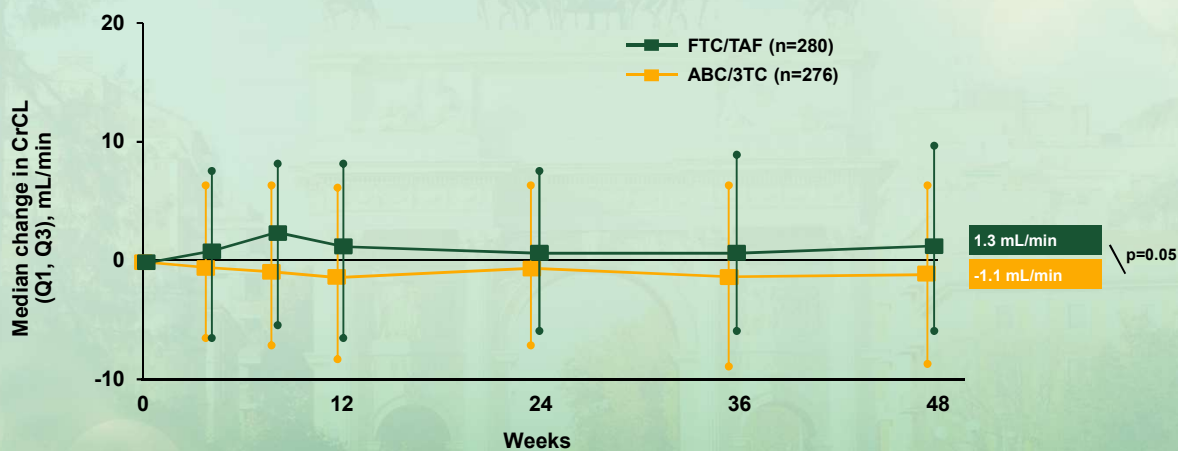
Winston A, et al. 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS84.

GS1717 STUDY: GRADE 3 TO 4 LAB ABNORMALITIES

≥2% in Either Group, %	FTC/TAF n=280	ABC/3TC n=276
Overall	22	18
LDL	5	5
Hyperbilirubinemia	5	3
Creatine kinase	3	4
Amylase	3	2
Hypercholesterolemia (fasting)	2	2

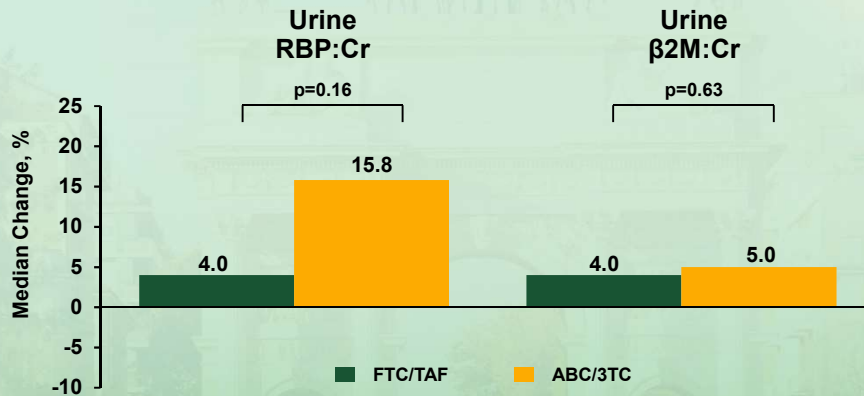
Winston A, et al; 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS84.

GS1717 STUDY: CHANGES IN CREATININE CLEARANCE (CRCL)



Winston A, et al; 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS84.

GS1717 STUDY: CHANGE IN RENAL BIOMARKERS



RBP, retinol-binding protein; beta2M, beta2-microglobulin.

Winston A, et al. 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS84.

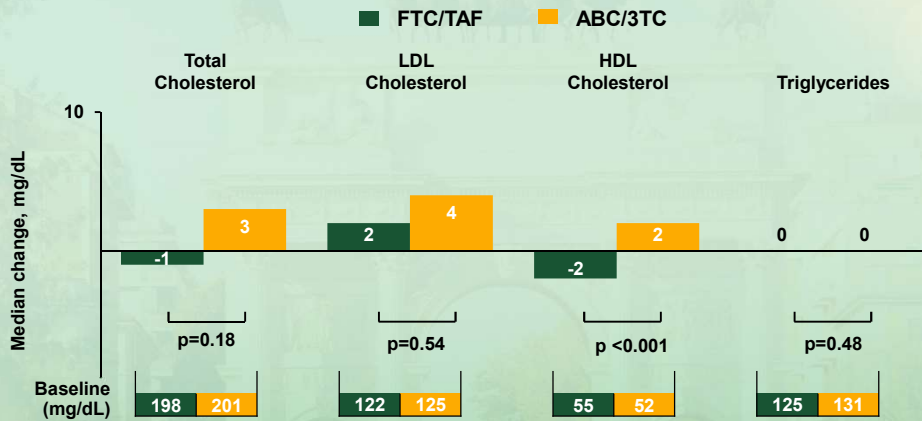
GS1717 STUDY: CHANGE IN BONE MINERAL DENSITY



FTC/TAF, n	256	238	213	253	235	212
ABC/3TC, n	251	237	217	248	233	212

Winston A, et al. 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS84.

GS1717 STUDY: CHANGE IN LIPIDS TO WEEK 48



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WEEK 48 CONCLUSIONS

In this 48-week analysis of a switch from ABC/3TC to FTC/TAF:

- FTC/TAF was noninferior to ABC/3TC in maintaining virologic suppression in combination with a variety of third agents
- No differences in renal and bone biomarkers vs ABC/3TC
 - Suggesting that TAF is kidney- and bone-neutral, similar to ABC
- No differences in lipid profile vs ABC/3TC
- In virologically suppressed patients with CrCL >50 mL/min, FTC/TAF provides an alternative backbone to ABC/3TC with similar effects on kidney and bone

Winston A, et al. 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS84.