ARV Therapies and Therapeutic Strategies
INDEPENDENT REPORTING ON EACS 2017

COMPREHENSIVE EXPERT REVIEW AND DISCUSSION OF KEY PRESENTATIONS
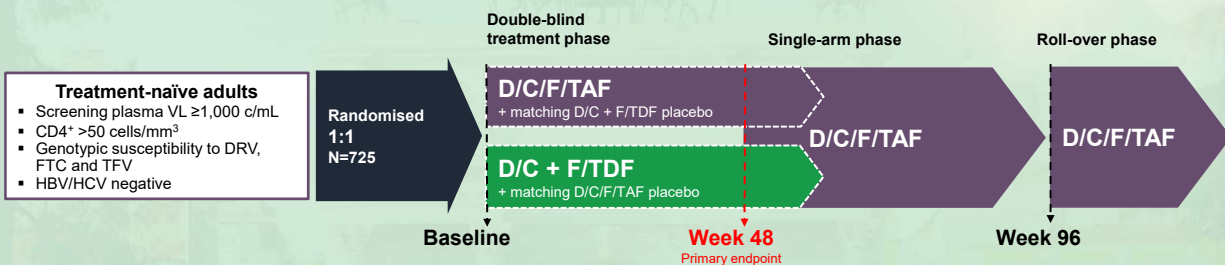
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WEEK 48 RESULTS OF AMBER: A PHASE 3, RANDOMISED, DOUBLE-BLIND TRIAL IN ANTIRETROVIRAL TREATMENT (ART)-NAÏVE HIV-1-INFECTED ADULTS TO EVALUATE THE EFFICACY AND SAFETY OF THE ONCE-DAILY, SINGLE-TABLET REGIMEN (STR) OF DARUNAVIR/ COBICISTAT/ EMTRICITABINE/ TENOFOVIR ALAFENAMIDE (D/C/F/TAF) VERSUS DARUNAVIR/COBICISTAT (DRV/C) PLUS EMTRICITABINE/ TENOFOVIR DISOPROXIL FUMARATE (FTC/TDF)

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Abstract PS8/2

AMBER STUDY: DESIGN

Treatment-naïve adults
- Screening plasma VL ≥1,000 c/mL
- CD4+ >50 cells/mm³
- Genotypic susceptibility to DRV, FTC and TFV
- HBV/HCV negative

Randomised 1:1 N=725

Double-blind treatment phase

D/C/F/TAF + matching D/C + F/TDF placebo

D/C + F/TDF + matching D/C/F/TAF placebo

Single-arm phase

D/C/F/TAF

Roll-over phase

D/C/F/TAF

Baseline

Week 48
Primary endpoint

Week 96

Primary Objective: Assess non-inferiority of D/C/F/TAF vs D/C + F/TDF by proportion of patients with VL <50 c/mL at 48 weeks (NI margin 10%; FDA-Snapshot algorithm)

Orkin C, et al; 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS8/2.

AMBER STUDY: BASELINE CHARACTERISTICS

	D/C/F/TAF QD N=362	Control N=363	Total N=725
Median (IQR) age, years	34 (27–42)	34 (27–42)	34 (27–42)
Male, n (%)	318 (87.8)	322 (88.7)	640 (88.3)
Median (IQR) $\log_{10}$ VL, c/mL	4.4 (4.0–4.8)	4.6 (4.2–4.9)	4.5 (4.1–4.9)
Median (IQR) CD4+ count, cells/mm³	461.5 (342–617)	440.0 (325–594)	453.0 (333–601)
Median (IQR) eGFR$_{cr}$, mL/min (Cockcroft-Gault)	119 (105–135)	118 (103–138)	119 (104–136.5)
Genotype at Screening	**N=361**	**N=362**	**N=723**
≥1 primary PI RAMs	7 (1.9)	8 (2.2)	15 (2.1)
≥1 NRTI RAMs	18 (5.0)	16 (4.4)	34 (4.7)
≥1 NNRTI RAMs	55 (15.2)	63 (17.4)	118 (16.3)

AMBER STUDY: VIROLOGIC OUTCOME AT WEEK 48
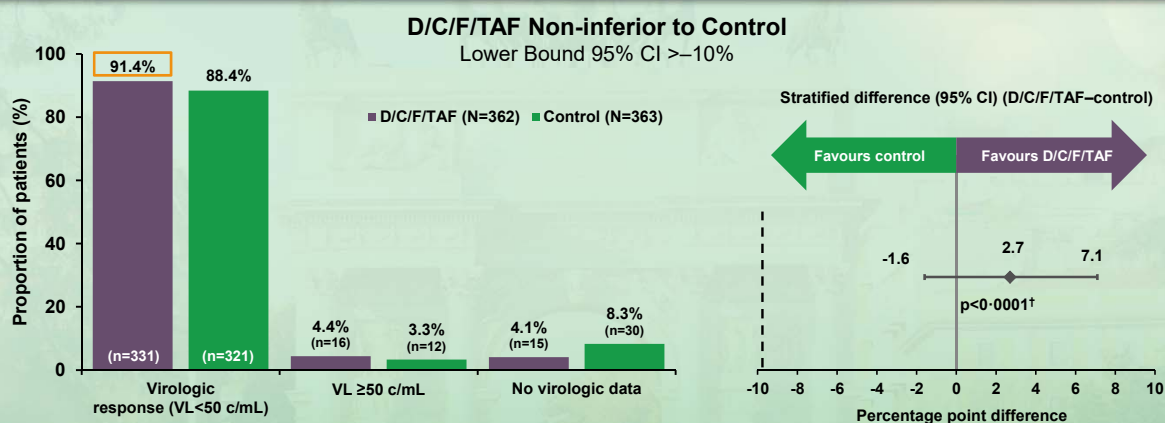
- Subgroup analysis by: Age, gender, race, CD4 (</>200), viral load (</> 100.000) similar results. Point estimates favor D/C/F/TAF

- No development of DRV, primary PI or TDF/TAF RAMs. One patient (D/C/F/TAF) developed M184I/V conferring resistance to FTC

† p-value for non-inferiority at 10% margin

AMBER STUDY: SAFETY

Incidence, n (%)	D/C/F/TAF QD N=362	Control N=363
≥1 AE, any grade	312 (86.2)	307 (84.6)
≥1 grade 3–4 AE	19 (5.2)	22 (6.1)
≥1 serious AE	17 (4.7)	21 (5.8)
Deaths	0	0
AEs Leading to Discontinuation		
≥1 AE	7 (1.9)	16 (4.4)
	Rash (n=6)	Rash/erythema (n=7)
	Diarrhoea (n=1)	Diarrhoea (n=1)
		Toxic skin eruption (n=2)
		SJS (n=1)
		Bone marrow oedema (n=1)
		Increased Beta 2 macroglobulin (n=1)
		Arthralgia (n=1)
		Neoplasms (n=2)

- Incidences and types of laboratory abnormalities were similar in both treatment arms being mostly Grade 1 or 2

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AMBER STUDY: MEAN CHANGES IN EGFR THROUGH 48 WEEKS

Estimated GFR based on Serum Creatinine[a]

D/C/F/TAF (N=340) Control (N=330)

p<0.0001*

Estimated GFR based on Serum Cystatin C[a]

D/C/F/TAF (N=337) Control (N=329)

p=0.001*
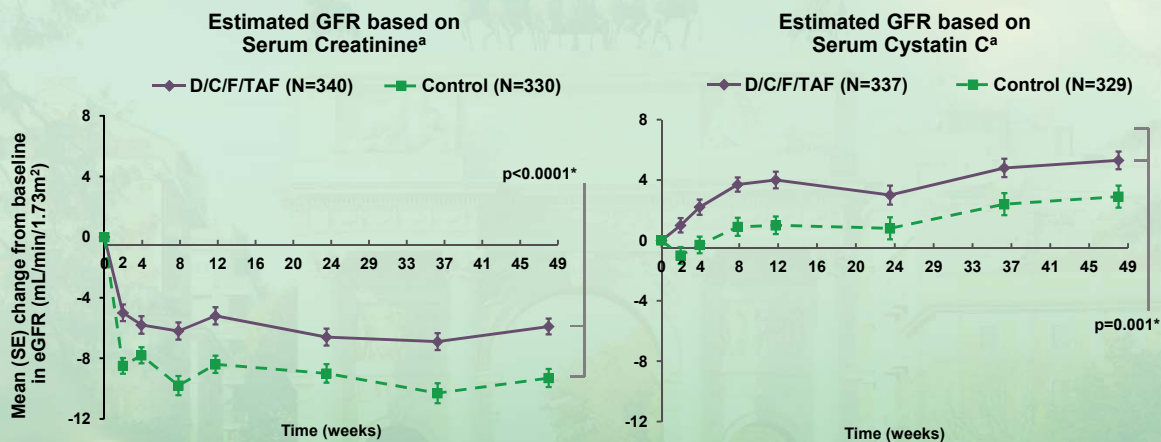
a. Based on serum levels and CKD-EPI formula
* p value for difference estimated using ANCOVA, including treatment as a factor and baseline eGFR as a covariate
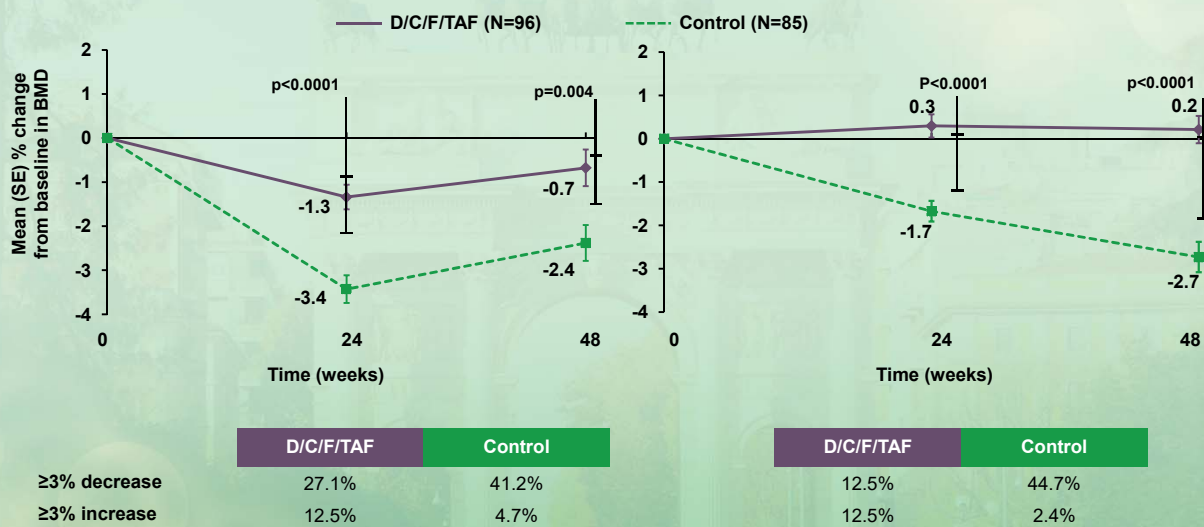
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## AMBER STUDY: MEAN CHANGES IN PROTEINURIA THROUGH 48 WEEKS

Urinary protein:creatinine

	D/C/F/TAF	Control
BL	66.23 (3.66)	77.67 (6.51)

D/C/F/TAF: -22.42
Control: -10.34
p=0.033

Urinary albumin:creatinine

	D/C/F/TAF	Control
BL	11.38 (1.57)	17.92 (5.07)

D/C/F/TAF: -2.45
Control: -0.58
p=0.003*

Retinol binding protein:creatinine

p<0.0001*

D/C/F/TAF: 16.84
Control: 401.12

	D/C/F/TAF	Control
BL	110.66 (7.12)	186.73 (74.66)

β-2-microglobulin:creatinine

p<0.0001*

D/C/F/TAF: -100.58
Control: 837.63

	D/C/F/TAF	Control
BL	248.45 (40.36)	379.54 (176.11)
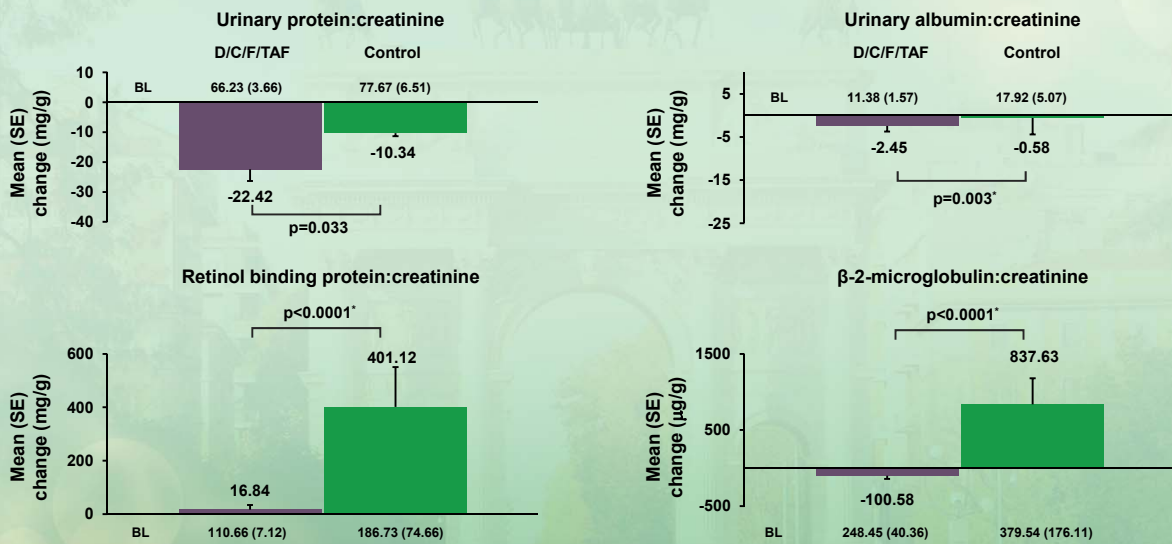
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AMBER STUDY: MEAN % CHANGES IN BMD THROUGH 48 WEEKS

D/C/F/TAF (N=96) — Control (N=85)

Left chart:
p<0.0001, p=0.004
-1.3, -0.7 (D/C/F/TAF)
-3.4, -2.4 (Control)

Right chart:
P<0.0001, p<0.0001
0.3, 0.2 (D/C/F/TAF)
-1.7, -2.7 (Control)

	D/C/F/TAF	Control		D/C/F/TAF	Control
≥3% decrease	27.1%	41.2%		12.5%	44.7%
≥3% increase	12.5%	4.7%		12.5%	2.4%

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AMBER STUDY: FASTING LIPID LEVELS AT BASELINE AND WEEK 48
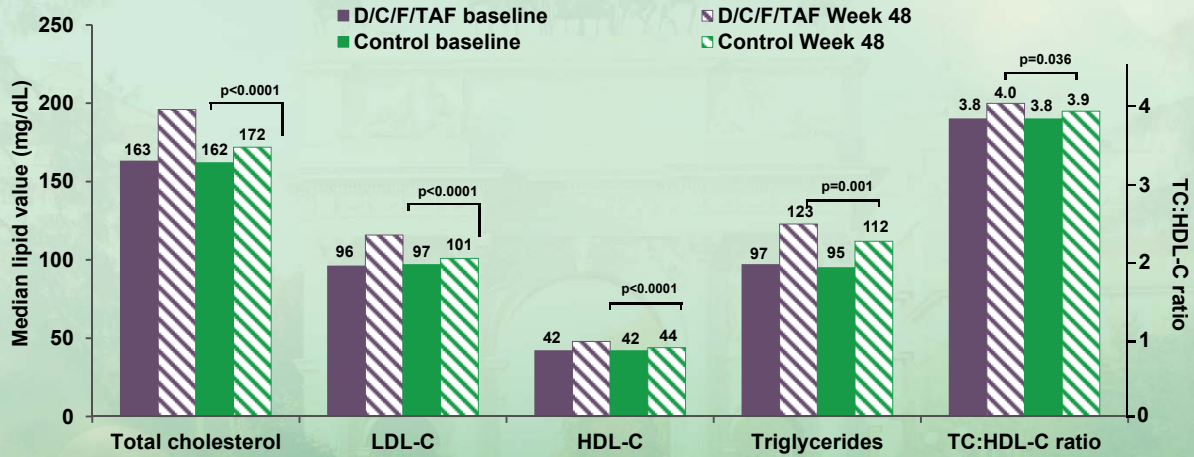
During treatment, lipid-lowering drugs started by 6 (1.7%) vs 2 (0.6%) patients (p=0.18)

Orkin C, et al; 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS8/2.