National HIV Curriculum

Darunavir-Cobicistat-Tenofovir Alafenamide-Emtricitabine (*Symtuza*)

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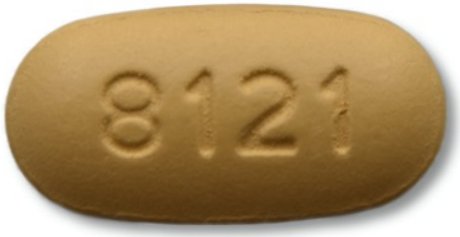
Darunavir-Cobicistat-Tenofovir Alafenamide-Emtricitabine



Darunavir-Cobicistat-Tenofovir alafenamide-Emtricitabine

800 mg	150 mg	10 mg	200 mg
PI	Booster	NRTI	NRTI

Dose: 1 tablet once daily with food

Source: Image courtesy of Janssen Therapeutics, Division of Janssen Products, LP

Darunavir-Cobicistat-Tenofovir Alafenamide-Emtricitabine Single-Tablet Regimen

- **Indication:** Complete regimen for treatment of HIV-1 in persons weighing ≥40 kg:
  - No prior antiretroviral treatment history, *or*
  - Virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable ART for ≥6 months and have no known resistance to darunavir or tenofovir
- **Dosing**: 1 pill daily with food
- **With Renal or Hepatic Impairment**
  - Not recommended if estimated CrCl <30 mL/min
  - Not recommended with severe hepatic impairment (Child-Pugh C)

Darunavir-Cobicistat-Tenofovir alafenamide-Emtricitabine Summary of Key Phase 3 Studies

- **Trials in Treatment-Naïve Adults**
  - AMBER: DRV-COBI-TAF-FTC versus DRV-COBI + TDF-FTC
- **Trials in Adults with Virologic Suppression**
  - EMERALD: Switch to DRV-COBI-TAF-FTC or stay on PI + TDF-FTC

Abbreviations: DRV-COBI-TAF-FTC = darunavir-cobicistat-tenofovir alafenamide-emtricitabine; DRV-COBI = darunavir-cobicistat; TDF-FTC = tenofovir DF-emtricitabine

Darunavir-Cobicistat-Tenofovir alafenamide-Emtricitabine

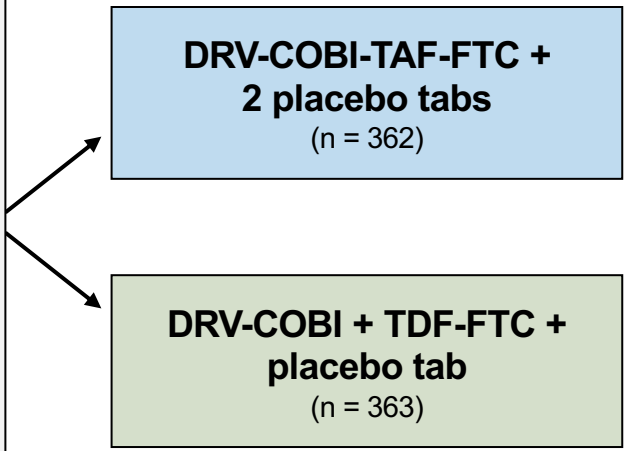
Trials in Treatment Treatment-Naïve Adults

DRV-COBI-TAF-FTC vs DRV-COBI + TDF-FTC

AMBER

DRV-COBI-TAF-FTC vs DRV-COBI + TDF-FTC as Initial ART
AMBER: Design

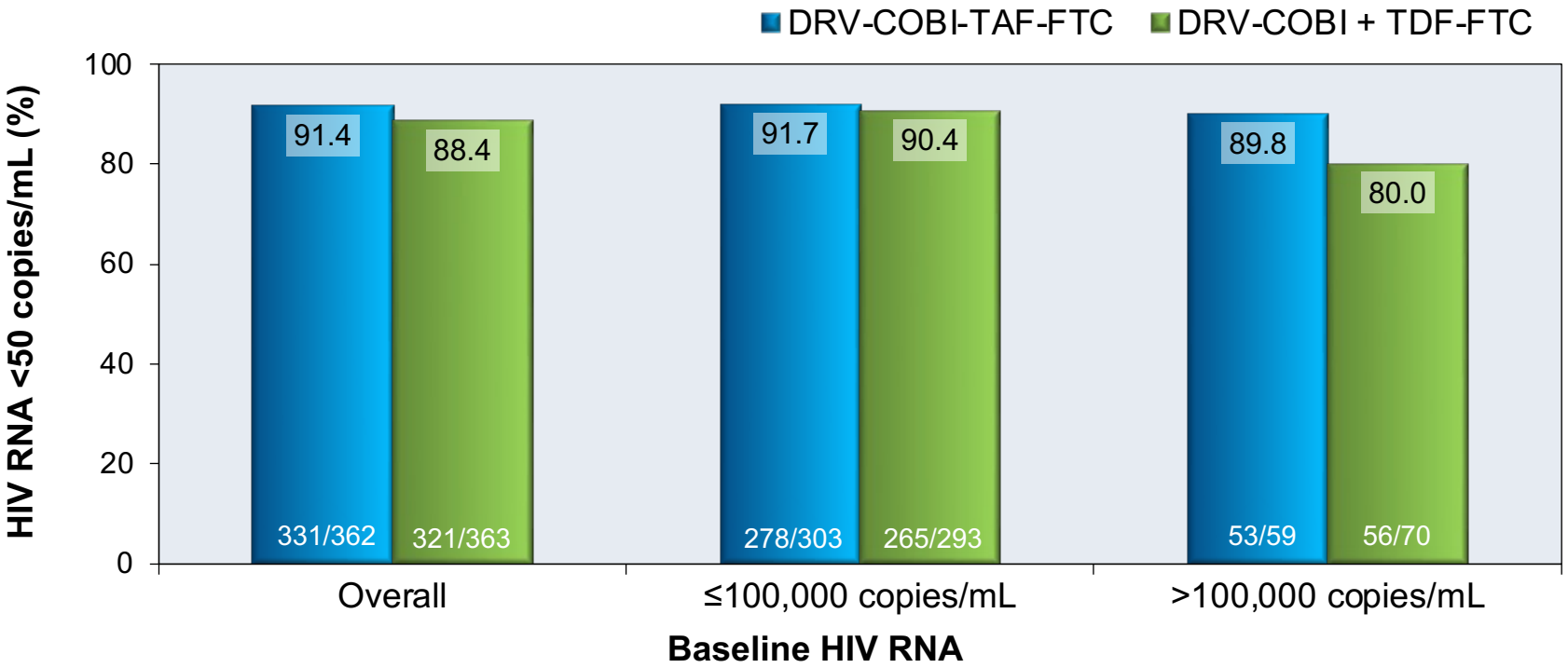
- **Background**: Randomized, double-blind, active-controlled, international, phase 3 study evaluating the efficacy and safety of the single-tablet regimen DRV-COBI-TAF-FTC compared with DRV-COBI + TDF-FTC for treatment-naïve individuals
- **Inclusion Criteria (n = 725)**
  - Age ≥18 years
  - Antiretroviral naïve
  - CD4 count >50 cells/mm^3
  - HIV RNA ≥1,000 copies/mL
  - eGFR ≥70 mL/min
  - Genotypic sensitivity to DRV, TDF, and FTC
  - No hepatitis B or C
  - Not pregnant
  - No AIDS-defining condition within 30 days



Source: Eron JJ, et al. AIDS. 2018;32:1431-42.

DRV-COBI-TAF-FTC vs DRV-COBI + TDF-FTC as Initial ART
AMBER: Results

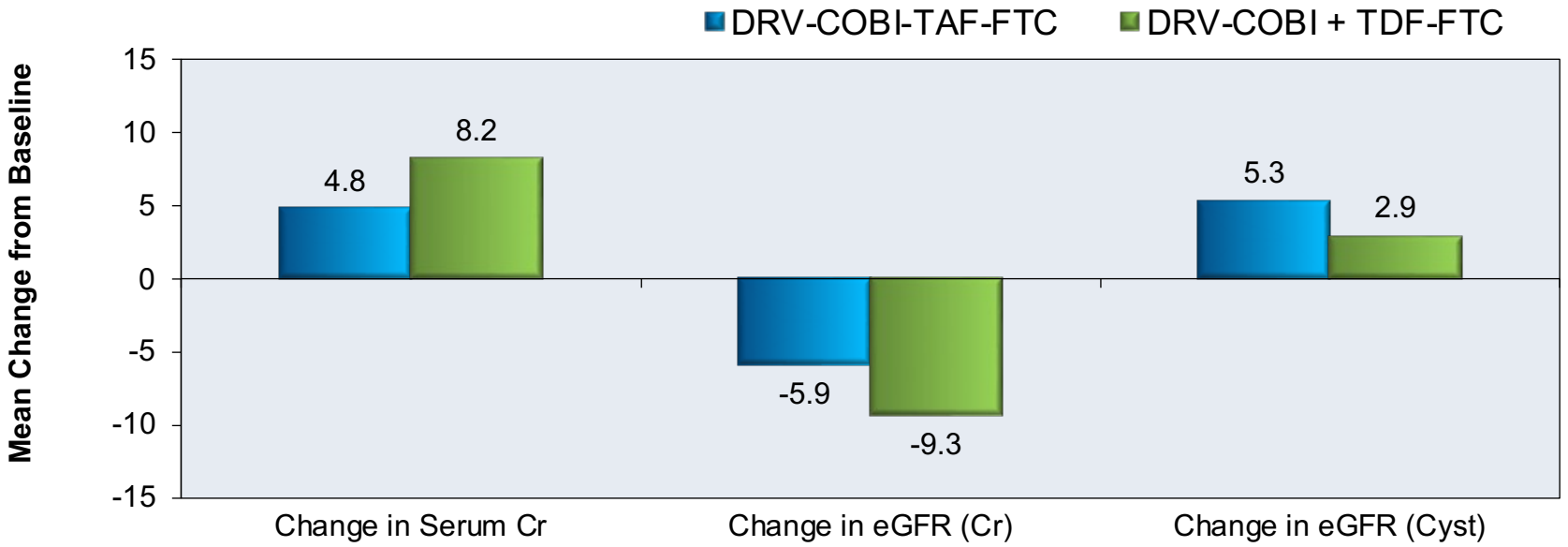
Week 48: Virologic Response by FDA Snapshot Analysis, ITT



Source: Eron JJ, et al. AIDS. 2018;32:1431-42.

DRV-COBI-TAF-FTC vs DRV-COBI + TDF-FTC as Initial ART
AMBER: Results

Week 48: Change in Serum Creatinine and Estimated GFR



Abbreviations: Cr = creatinine (measured in µmol/L); eGFR = estimated glomerular filtration rate (measured in mL/min/1.73m^2, calculated using CKD-EPI); Cyst = cystatin C

Source: Eron JJ, et al. AIDS. 2018;32:1431-42.

DRV-COBI-TAF-FTC vs DRV-COBI + TDF-FTC as Initial ART
AMBER: Results

Week 48: Change in Urinary Markers of Tubular Dysfunction

Mean Change in Markers of Proximal Tubulopathy at Week 48

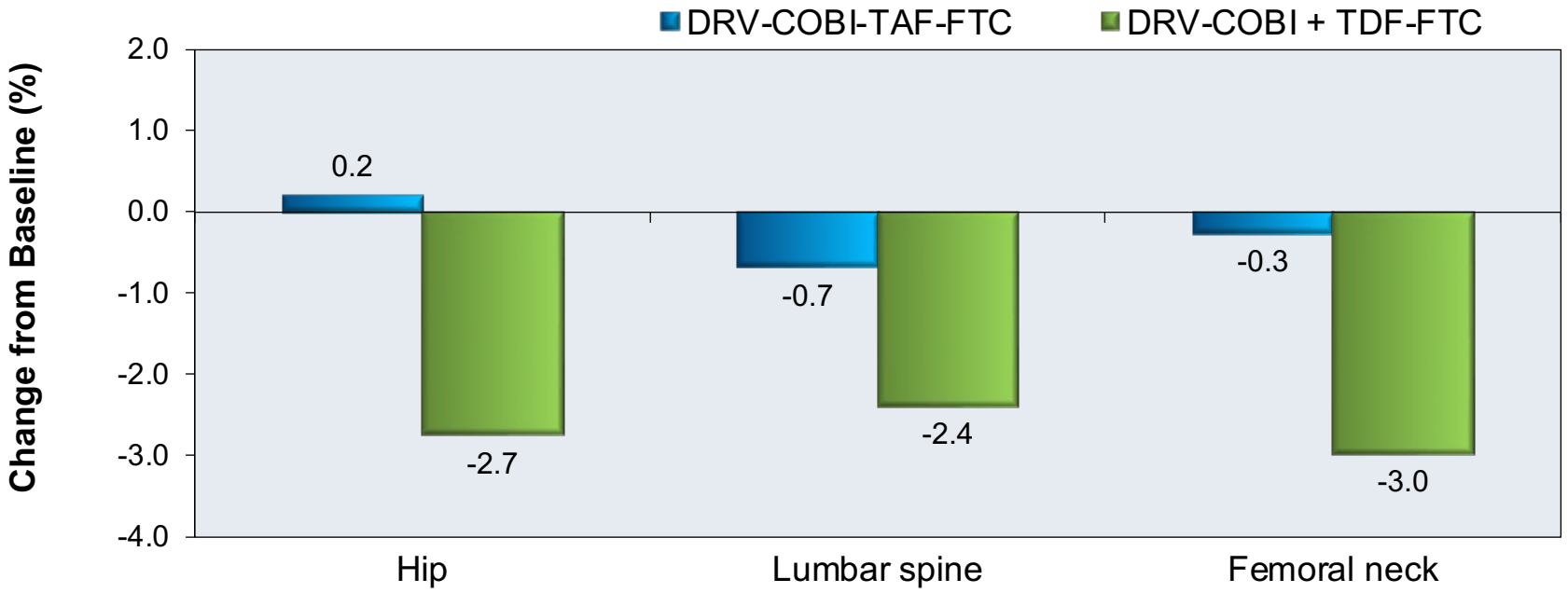
	DRV-COBI-TAF-FTC (n = 362)	DRV-COBI + TDF-FTC (n = 363)
UPCR (mg/g)	-22.42	-10.34
UACR (mg/g)	-2.45	-0.58
RBP:Cr (µg/g)	16.84	401.12
β2M:Cr (µg/g)	-100.58	837.63

UPCR = urine protein to creatinine ratio; UACR = urine albumin to creatinine ratio
RBP:Cr = retinol binding protein to creatinine ratio; β2M:Cr = beta-2-microglobulin to creatinine ratio

Source: Eron JJ, et al. AIDS. 2018;32:1431-42.

DRV-COBI-TAF-FTC vs DRV-COBI + TDF-FTC as Initial ART
AMBER: Results

Week 48: Percentage Change in Bone Mineral Density*



*This is from a bone mineral density substudy (n = 113 participants in TAF arm, 99 in control arm)

Source: Eron JJ, et al. AIDS. 2018;32:1431-42.

DRV-COBI-TAF-FTC vs DRV-COBI + TDF-FTC as Initial ART
AMBER: Results

Median Change in Fasting Lipid Parameters at Week 48

	DRV-COBI-TAF-FTC (n = 362)	DRV-COBI + TDF-FTC (n = 363)
TC (mg/dL)	28.6	10.4
LDL (mg/dL)	17.4	5.0
HDL (mg/dL)	4.3	1.5
TC:HDL ratio	0.2	0.08
Triglycerides (mg/dL)	23.9	14.2

TC = total cholesterol; LDL = low density lipoprotein; HDL = high density lipoprotein

Source: Eron JJ, et al. AIDS. 2018;32:1431-42.

DRV-COBI-TAF-FTC vs DRV-COBI + TDF-FTC as Initial ART
AMBER: Results

Conclusions: “Darunavir-cobicistat-emtricitabine-tenofovir alafenamide achieved a high virologic suppression rate (91.4%) and was noninferior to darunavir-cobicistat with emtricitabine-tenofovir DF. Darunavir-cobicistat-emtricitabine-tenofovir alafenamide also demonstrated the bone and renal safety advantages of tenofovir alafenamide in combination with darunavir-cobicistat.”

Source: Eron JJ, et al. AIDS. 2018;32:1431-42.

Darunavir-Cobicistat-Tenofovir alafenamide-Emtricitabine

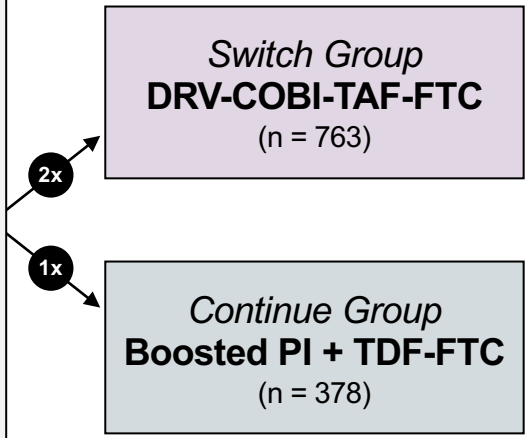
Switch Studies in Adults with Virologic Suppression

DRV-COBI-TAF-FTC vs Continue Boosted PI + TDF-FTC

EMERALD

DRV-COBI-TAF-FTC vs Continue Boosted PI + TDF-FTC
EMERALD: Design

- **Background**: Randomized, open-label, active-controlled, international, phase 3 study evaluating the efficacy and safety of switching to the single-tablet regimen DRV-COBI-TAF-FTC versus continuing a boosted PI + TDF-FTC
- **Inclusion Criteria (n = 1,141)**
  - Age ≥18 years
  - Antiretroviral experienced
  - HIV RNA ≤50 copies/mL for >2 months*
  - Taking a PI plus ritonavir or cobicistat
  - Regimen stable for ≥6 months
  - eGFR ≥50 mL/min
  - No prior virologic failure on a DRV-based regimen
  - Virologic failure on non-DRV-based regimen allowed
  - Not pregnant or breastfeeding



*One HIV RNA 50-200 copies/mL within prior 12 months allowed

Source: Orkin C, et al. Lancet HIV. 2018;5:e23-e34.

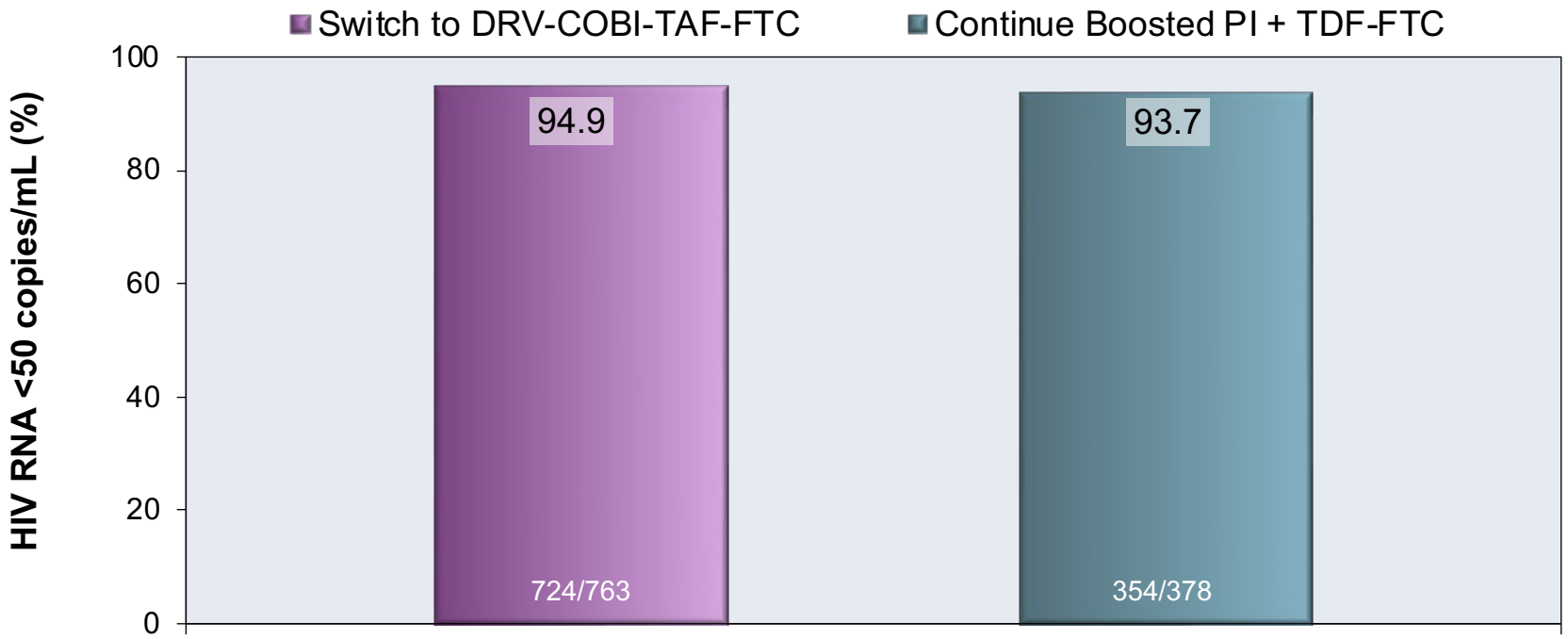
DRV-COBI-TAF-FTC vs Continue a Boosted PI + TDF-FTC
EMERALD: Baseline Characteristics

EMERALD Study: Baseline Characteristics	DRV-COBI-TAF-FTC *Switch Group* (n = 763)	Boosted PI + TDF-FTC *Continue Group* (n = 378)
CD4 Count (cells/mL)	630	624
Time since HIV diagnosis (years)	9.3	8.9
Time since first ART (years)	6.2	5.8
Previous use of >5 ARV's	59	58
Previous virologic failure	15	14
Boosted darunavir at screening (%)	70	70
Boosted atazanavir at screening (%)	22	22
Boosted lopinavir at screening (%)	8	8

Source: Orkin C, et al. Lancet HIV. 2018;5:e23-e34.

DRV-COBI-TAF-FTC vs Continue a Boosted PI + TDF-FTC
EMERALD: Results

Week 48: Virologic Response by FDA Snapshot Analysis, ITT



Source: Orkin C, et al. Lancet HIV. 2018;5:e23-e34.

DRV-COBI-TAF-FTC vs Continue a Boosted PI + TDF-FTC
EMERALD: Results

Week 48: Virologic Outcomes

EMERALD Study Virologic Outcomes

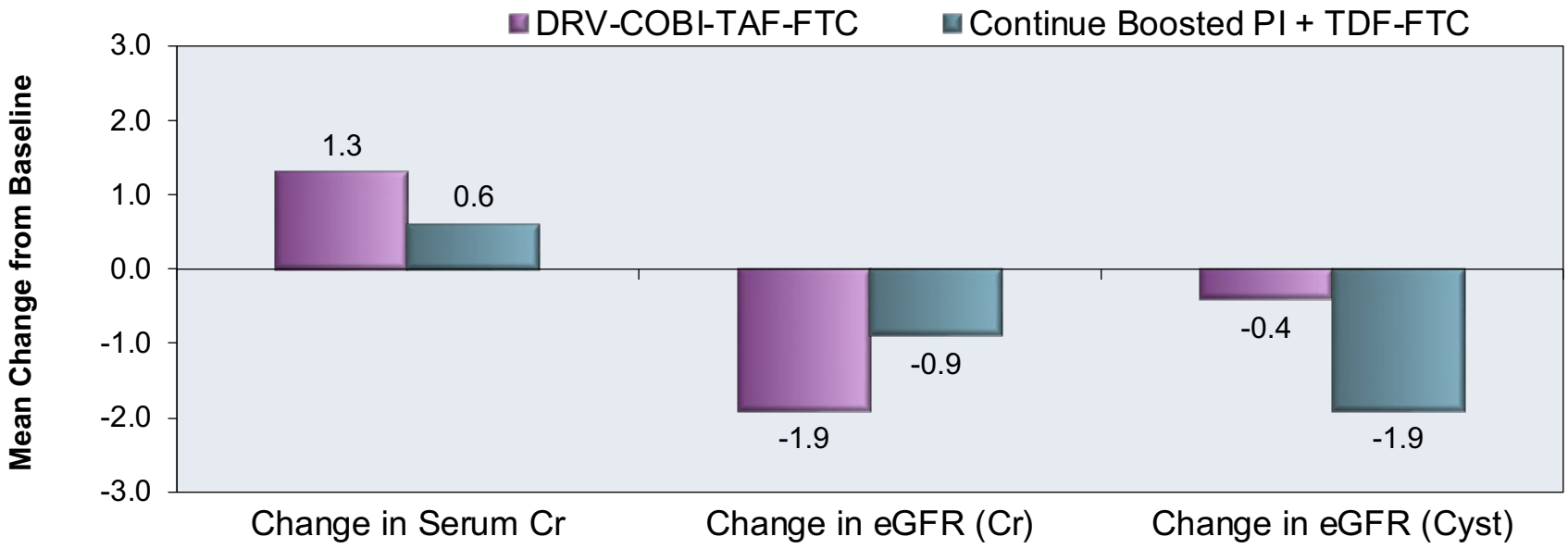
	DRV-COBI-TAF-FTC *Switch Group* (n = 763)	Boosted PI + TDF-FTC *Continue Group* (n = 378)
Virologic rebound rate through 48 weeks*	2.5%	2.1%
HIV RNA <50 copies/mL at 48 weeks	94.9%	93.7%
HIV RNA ≥50 copies/mL at 48 weeks	0.8%	0.5%
No virologic data at 48 weeks	4.3%	5.8%

*HIV RNA ≥50 copies/mL or premature discontinuation with last HIV RNA ≥50copies/mL

Source: Orkin C, et al. Lancet HIV. 2018;5:e23-e34.

DRV-COBI-TAF-FTC vs Continue a Boosted PI + TDF-FTC
EMERALD: Results

Week 48: Change in Serum Creatinine and Estimated GFR



Cr = creatinine (measured in µmol/L)
eGFR = estimated glomerular filtration rate (measured in mL/min/1.73 m^2, calculated using CKD-EPI)
Cyst = cystatin C

Source: Orkin C, et al. Lancet HIV. 2018;5:e23-e34.

DRV-COBI-TAF-FTC vs Continue a Boosted PI + TDF-FTC
EMERALD: Results

Week 48: Change in Urinary Markers of Tubular Dysfunction

Mean Change in Markers of Proximal Tubulopathy at Week 48

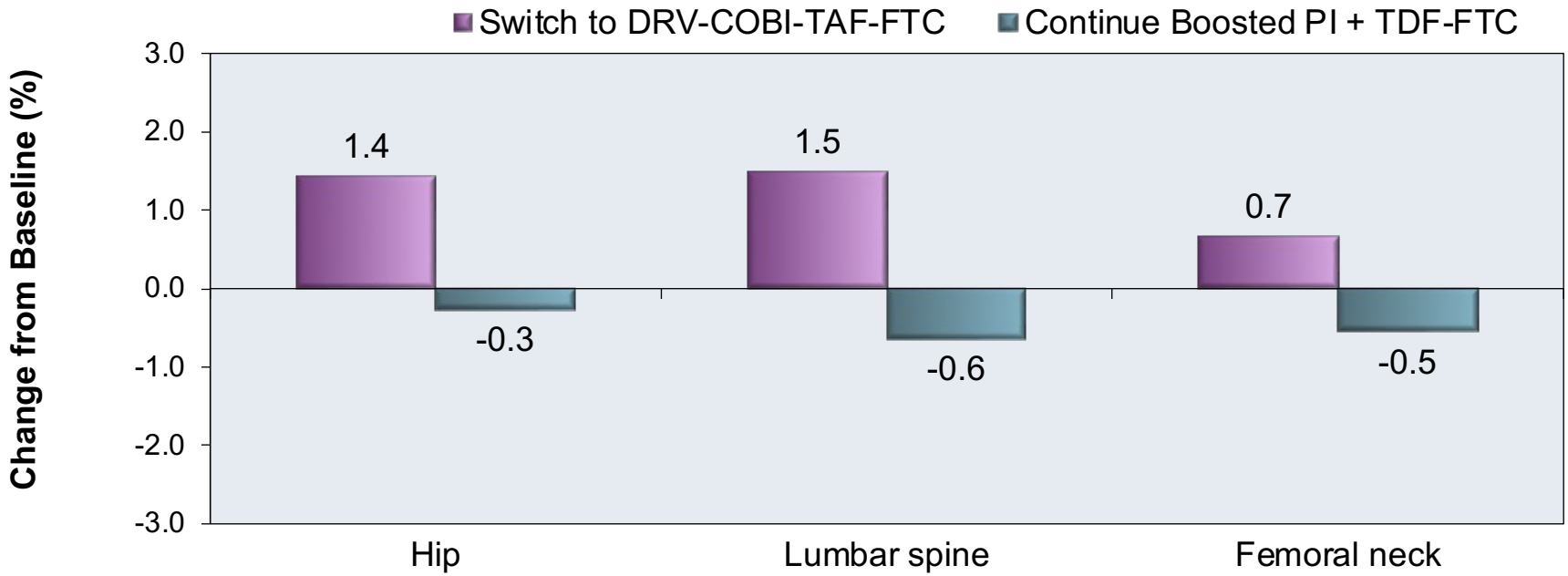
	DRV-COBI-FTC-TAF *Switch Group* (n = 763)	Boosted PI + TDF-FTC *Continue Group* (n = 378)
UPCR (mg/g)	-33.9	-6.43
UACR (mg/g)	-3.2	1.3
RBP:Cr (mg/g)	-630.5	1037.1
β2M:Cr (mg/g)	-1454.7	1371.3

UPCR = urine protein to creatinine ratio; UACR = urine albumin to creatinine ratio
RBP:Cr = retinol binding protein to creatinine ratio; β2M:Cr = beta-2-microglobulin to creatinine ratio

Source: Orkin C, et al. Lancet HIV. 2018;5:e23-e34.

DRV-COBI-TAF-FTC vs Continue a Boosted PI + TDF-FTC
EMERALD: Results

Week 48: Change in Bone Mineral Density



This is from a bone mineral density substudy (n = 209 participants in switch arm, 108 in control arm)

Source: Orkin C, et al. Lancet HIV. 2018;5:e23-e34.

DRV-COBI-TAF-FTC vs Continue a Boosted PI + TDF-FTC
EMERALD: Results

Median Change in Fasting Lipid Parameters at Week 48

	DRV-COBI-FTC-TAF *Switch Group* (n = 763)	Boosted PI + TDF-FTC *Control Group* (n = 378)
TC (mg/dL)	19.7	1.3
LDL (mg/dL)	15.7	1.9
HDL (mg/dL)	3.0	-1.0
TC:HDL ratio	0.2	0.1
Triglycerides (mg/dL)	6.0	5.0

TC = total cholesterol; LDL = low density lipoprotein; HDL = high density lipoprotein

Source: Orkin C, et al. Lancet HIV. 2018;5:e23-e34.

DRV-COBI-TAF-FTC vs Continue a Boosted PI + TDF-FTC
EMERALD: Conclusions

Conclusions: “Our findings show the safety and efficacy of single-tablet darunavir, cobicistat, emtricitabine, and tenofovir alafenamide as a potential switch option for the treatment of HIV-1 infection in adults with viral suppression.”

Source: Orkin C, et al. Lancet HIV. 2018;5:e23-e34

Acknowledgments

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AETC AIDS Education & Training Center Program

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