ARV Therapies and Therapeutic Strategies

INDEPENDENT REPORTING ON IAS 2017

COMPREHENSIVE EXPERT REVIEW AND DISCUSSION OF KEY PRESENTATIONS

EFFICACY AND SAFETY OF SWITCHING FROM BOOSTED-PROTEASE INHIBITOR PLUS EMTRICITABINE/TENOFOVIR DISOPROXIL FUMARATE REGIMENS TO THE SINGLE-TABLET REGIMEN OF DARUNAVIR/COBICISTAT/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (D/C/F/TAF) IN VIROLOGICALLY-SUPPRESSED, HIV-1-INFECTED ADULTS THROUGH 24 WEEKS: EMERALD STUDY

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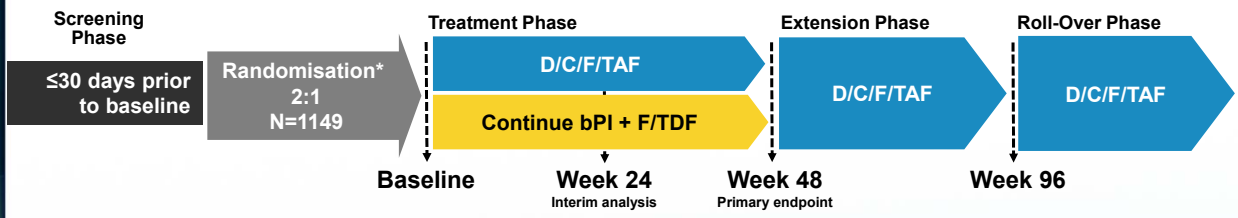
Abstract TUAB0101

EMERALD: STUDY DESIGN



- Previous ART VF allowed
- Absence of history of VF on DRV, and if historical genotype available, absence of DRV RAMs
- Viral load (VL) <50 c/mL for ≥2 months before screening; one VL ≥50 and <200 c/mL within 12 months prior to screening allowed
- Creatinine clearance (by Cockcroft-Gault) ≥50 mL/min

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EMERALD STUDY: BASELINE CHARACTERISTICS

	D/C/F/TAF QD N=763	Control N=378
Female, n (%)	140 (18.3)	65 (17.2)
Median (range) age, years	46 (19–75)	45 (20–78)
Median (range) CD4+ cell count, cells/mm^3	630 (111–1921)	624 (131–1764)
Median (range) time since diagnosis, years	9.3 (0.6–35.0)	8.9 (0.6–32.6)
On first ARV regimen, n (%)	317 (41.6)	160 (42.6)
Prior VF, n (%)	116 (15.2)	53 (14.1)
Boosted PI at screening, n (%)		
DRV	540 (70.8)	266 (70.4)
ATV	164 (21.5)	82 (21.7)
LPV	59 (7.7)	30 (7.9)
COBI, n (%)	107 (14.0)	65 (17.2)
eGFR creatinine (Cockcroft-Gault), Mean (SD)	107.5 (30.56)	107.0 (30.29)

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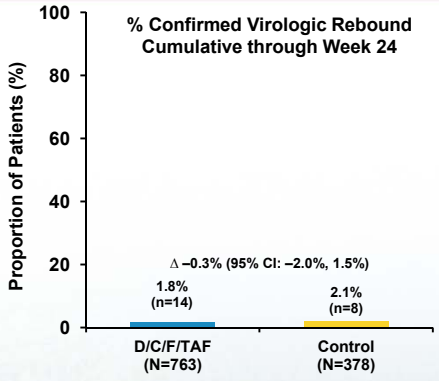
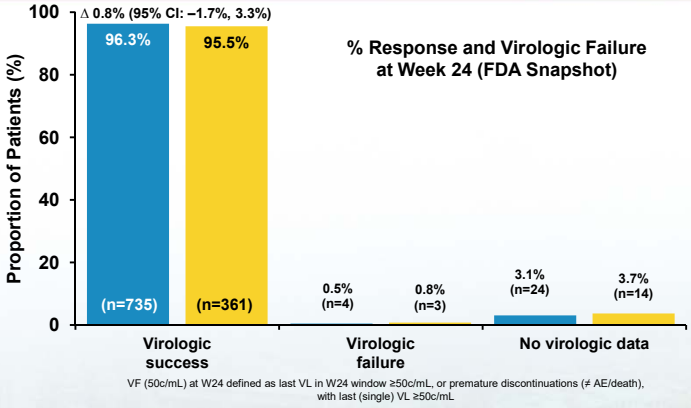
EMERALD STUDY: EFFICACY





VF (50c/mL) at W24 defined as last VL in W24 window ≥50c/mL, or premature discontinuations (≠ AE/death), with last (single) VL ≥50c/mL

- Most rebounders (10/14 D/C/F/TAF and 5/8 control) resuppressed (<50c/mL) by Week 24
- No confirmed rebounds ≥200 c/mL
- No discontinuations for VF
- No DRV/primary PI or NRTI RAMs were observed (2 patients genotyped in each group)

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EMERALD STUDY: ADVERSE EVENTS THROUGH 24 WEEKS

	D/C/F/TAF QD N=763	Control N=378
Incidence, n (%)		
≥1 AE, any grade, regardless of causality	543 (71.2)	265 (70.1)
≥1 grade 3–4 AE related to study drug	9 (1.2)	2 (0.5)
≥1 serious AE	19 (2.5)	12 (3.2)
Total discontinuations	22 (2.9)	11 (2.9)
≥1 AE leading to permanent discontinuation	10 (1.3)	4 (1.1)
Discontinuations due to renal AEs	1 (0.1)	2 (0.5)
Deaths	0	0
Most common AEs (≥5% both arms)		
Nasopharyngitis	58 (7.6)	25 (6.6)
Upper respiratory tract infection	48 (6.3)	24 (6.3)
Vitamin D deficiency	42 (5.5)	19 (5.0)

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EMERALD STUDY: SAFETY GRADE 3 OR 4 LABORATORY ABNORMALITIES THROUGH WEEK 24

Parameter, n (%)	D/C/F/TAF QD N=763	Control N=378
Creatinine clearance[a] (<60 mL/min)	31 (4.1)	12 (3.2)
Fasting LDL-C (≥4.90 mmoL/L)	23 (3.0)	2 (0.5)
Phosphate (<0.65 mmoL/L)	15 (2.0)	15 (4.0)
Creatinine kinase (≥10 x ULN)	10 (1.3)	8 (2.1)
Total bilirubin (≥2.6 x ULN)	1 (0.1)	16 (4.3)

- No clinically or statistically significant difference between arms in median change from baseline to Week 24 in TC/HDL-C ratio (D/C/F/TAF 0.2 vs control 0.1; p=0.288*)

Worst grade, treatment-emergent grade 3 or 4 events occurring in ≥2% of patients in either arm
*Assessed by van Elteren test, controlling for bPI at screening

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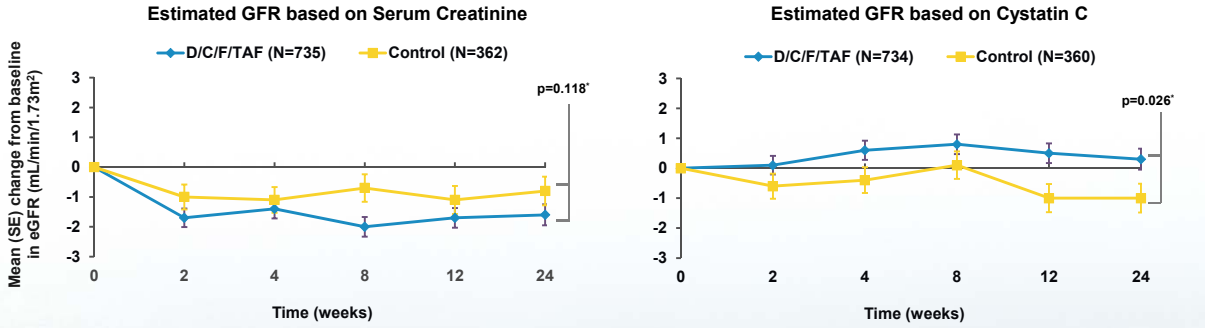
EMERALD STUDY: SAFETY



	D/C/F/TAF QD N=763	Control N=378
Total Discontinuations	22 (2.9)	11 (2.9)
≥1 AE leading to permanent discontinuation	10 (1.3)	4 (1.1)
Discontinuations due to renal AEs	1 (0.1)	2 (0.5)
Deaths	0	0

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EMERALD WEEK 24 ANALYSIS: CONCLUSIONS

- Through Week 24, switching from bPI + FTC/TDF to D/C/F/TAF resulted in:
  - Low virologic rebound rate cumulative through 24 weeks (1.8%)
  - High virologic suppression rate (96.3%)
  - No discontinuations for VF
  - No resistance to any study drug
  - Few serious AEs and discontinuations due to AEs
- D/C/F/TAF bone, renal and lipid safety vs control were consistent with known profiles of TAF and cobicistat

D/C/F/TAF combines the safety advantages of TAF and DRV, with the known efficacy and high genetic barrier to resistance of DRV, in an STR

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