HIV Treatment-experienced Patients Switched to D/C/F/TAF: Age, Gender, and Race Analyses

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INTRODUCTION

- The oral, once-daily, single-tablet regimen darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) 800/150/200/10 mg is approved in Europe[1] and under regulatory review in the United States for the treatment of human immunodeficiency virus (HIV)–1 infection[2]
- The efficacy and safety of darunavir (DRV) have been demonstrated in individuals living with HIV-1 infection[3]; DRV has also shown a high barrier to resistance, most recently in an analysis of 7 clinical trials of DRV 800 mg once daily, with study durations of up to 192 weeks.[4] Compared with tenofovir disoproxil fumarate (TDF), the tenofovir prodrug TAF has shown similar efficacy and improved renal and bone safety[5,6]
- D/C/F/TAF has been evaluated in pivotal phase 3 trials of both treatment-experienced, virologically suppressed (EMERALD) and treatment-naïve (AMBER) patients.[7,8] In the EMERALD trial, switching to D/C/F/TAF was noninferior to continuing use of a boosted protease inhibitor (bPI) + emtricitabine (FTC)/TDF for virologic rebound through 48 weeks[7]

OBJECTIVE

- To evaluate efficacy and safety results from the EMERALD trial of treatment-experienced patients receiving D/C/F/TAF across subgroups based on age, gender, and race

METHODS

Study Design

- EMERALD is an ongoing phase 3, randomized, noninferiority trial of treatment-experienced, virologically suppressed adults with HIV-1 infection (**Figure 1**)[7]
  - Patients must have had a viral load (VL) <50 HIV-1 RNA copies/mL for 12 to 2 months prior to screening; one 50< VL <200 copies/mL within 12 months prior to screening was allowed
  - Previous non-DRV virologic failure (VF) was allowed
  - There was no restriction on resistance-associated mutations (RAMs) at screening, except that DRV RAMs were not allowed (if historical genotype was available)

Figure 1. EMERALD study design.

eGFR, estimated glomerular filtration rate; rtv, ritonavir; COBI, cobicistat; IAS-USA, International Antiviral Society–USA.
*Stratified by bPI (PI boosted with low-dose rtv or COBI) at screening.
†Prior use of boosted DRV was allowed.
‡IAS-USA DRV RAMs.
§bPI was atazanavir with rtv or COBI, DRV with rtv or COBI, or lopinavir with rtv.

Analyses

- The primary endpoint in EMERALD was the proportion of patients with cumulative virologic rebound through Week 48
  - Virologic rebound was defined as confirmed VL ≥50 copies/mL or premature discontinuation with last VL ≥50 copies/mL
- Efficacy was assessed by virologic response, defined as VL <50 copies/mL (US Food and Drug Administration [FDA] snapshot)
- The difference (95% confidence interval [CI]) between the D/C/F/TAF and control groups for virologic rebound and virologic response was calculated as follows:
  - Overall population: Mantel–Haenszel test adjusted for bPI at screening (atazanavir with rtv or COBI, DRV with rtv or COBI, lopinavir with rtv)
  - Subgroups: exact CIs
- Safety was assessed by adverse events (AEs) and changes in bone mineral density (BMD) and eGFR (calculated using serum cystatin C [Chronic Kidney Disease Epidemiology Collaboration formula]) from baseline to Week 48
- Analyses were performed in the intention-to-treat population (all randomized patients who received ≥1 dose of study drug)
- Results were evaluated in subgroups by age (≤50 vs >50 years), gender, and race (black/African American vs non-black/African American)
  - Patients with race categorized as "unknown" or "not reported" were not included in the analysis of race subgroups

RESULTS

Patient Population

- Overall, baseline demographic characteristics were generally similar in the D/C/F/TAF and control groups (**Table 1**)[7]

Table 1. Baseline Demographic and Clinical Characteristics (Overall Population)

Parameter	D/C/F/TAF (N = 763)	Control (N = 378)
Demographic characteristics		
Age, median (range), y	46 (19-75)	45 (20-78)
Age category, n (%)		
≤50 y	507 (66)	252 (67)
>50 y	256 (34)	126 (33)
Gender, n (%)		
Men	623 (82)	313 (83)
Women	140 (18)	65 (17)
Race, n (%)*		
Non-black/African American	597 (79)	293 (78)
Black/African American	155 (21)	82 (22)
Clinical characteristics		
Time since diagnosis, median (range), y	9 (1-35)	9 (1-33)
Time since first ARV therapy, median (range), y	6 (1-33)	6 (1-28)
≥5 prior ARVs (including screening ARVs), n (%)†	447 (59)	217 (57)
≥1 prior VF, n (%)	116 (15)	53 (14)
CD4+ cell count, median (range), cells/μL‡	630 (111-1,921)	624 (131-1,764)

ARV, antiretroviral.
*Percentages calculated excluding patients with "unknown" or "not reported" race.
†PI booster counted as a separate ARV.
‡CD4+ cell count data at baseline.

Efficacy

- Virologic rebound rates were similar in the D/C/F/TAF and control arms in the overall population, and results were consistent across age, gender, and race subgroups (**Figure 2**)
- Virologic response rates were also similar in the D/C/F/TAF and control arms, overall and across subgroups (**Figure 3**)

Resistance

- Among the few patients with virologic rebound, 4 had available genotype data (1 in the D/C/F/TAF arm and 3 in the control arm)
- No resistance to study drugs was observed in any arm across subgroups[7]

Safety

- The incidence of AEs was similar in the D/C/F/TAF and control arms in the overall population, with consistent results across subgroups (**Table 2**)
  - Rates of discontinuation due to AEs and serious AEs were low for D/C/F/TAF and control, overall and across subgroups
- Overall, the most common study drug–related AEs (≥2% in either arm) were diarrhea (D/C/F/TAF: 16 [2%]; control: 3 [1%]) and osteopenia (D/C/F/TAF: 5 [1%]; control: 8 [2%])
- Three patients had a study drug–related, clinical, renal AE of interest: 1 (<1%) in the D/C/F/TAF arm and 2 (1%) in the control arm
- Improvements in markers of proteinuria (β-2 microglobulin:creatinine ratio and urine albumin:creatinine ratio) were observed with D/C/F/TAF relative to control in the overall population and across subgroups at Week 48 (**Figure 4**)
- Lower rates of bone AEs of interest and increases in BMD were observed with D/C/F/TAF versus control, overall and across subgroups (**Table 3** and **Figure 5**)
  - There were no fractures unrelated to trauma in any arm across subgroups

Figure 2. Virologic rebound through Week 48.

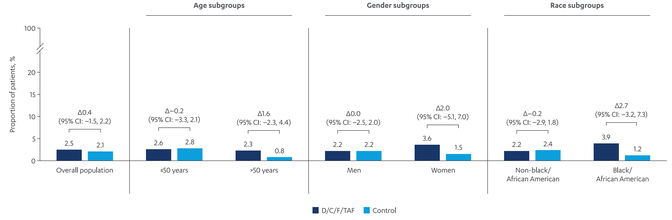
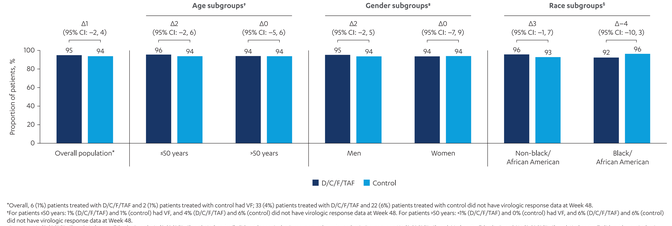
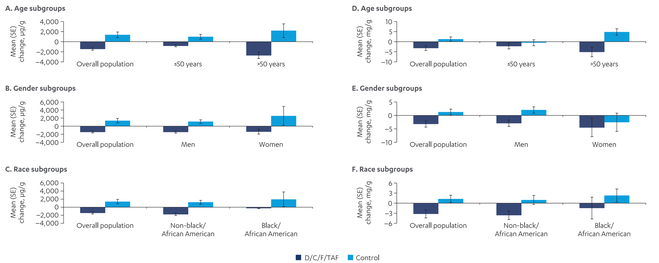


Figure 3. Virologic response at Week 48.



*Overall, 6 (1%) patients treated with D/C/F/TAF and 2 (1%) patients treated with control had VF; 33 (4%) patients treated with D/C/F/TAF and 22 (6%) patients treated with control did not have virologic response data at Week 48.
†For patients ≤50 years: 1% (D/C/F/TAF) and 1% (control) had VF, and 4% (D/C/F/TAF) and 6% (control) did not have virologic response data at Week 48. For patients >50 years: 4% (D/C/F/TAF) and 0% (control) had VF, and 6% (D/C/F/TAF) and 6% (control) did not have virologic response data at Week 48.
‡For men: 1% (D/C/F/TAF) and 1% (control) had VF, and 4% (D/C/F/TAF) and 6% (control) did not have virologic response data at Week 48. For women: 1% (D/C/F/TAF) and 0% (control) had VF, and 5% (D/C/F/TAF) and 6% (control) did not have virologic response data at Week 48.
§For non-black/African American patients: 1% (D/C/F/TAF) and 1% (control) had VF, and 4% (D/C/F/TAF) and 7% (control) did not have virologic response data at Week 48. For black/African American patients: 1% (D/C/F/TAF) and 0% (control) had VF, and 7% (D/C/F/TAF) and 4% (control) did not have virologic response data at Week 48.

Figure 4. Changes from baseline to Week 48 in renal laboratory parameters.



SE, standard error.

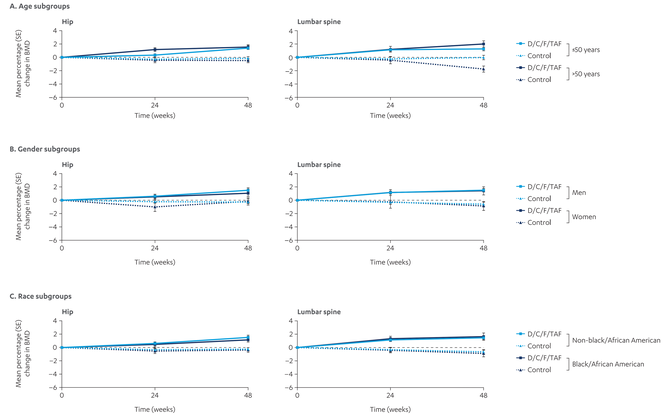
Table 2. Incidence (%) of AEs Through Week 48

	Overall population		Age subgroups				Gender subgroups				Race subgroups			
			≤50 years		>50 years		Men		Women		Non-black/ African American		Black/ African American	
Parameter, %	D/C/F/TAF	Control	D/C/F/TAF	Control	D/C/F/TAF	Control	D/C/F/TAF	Control	D/C/F/TAF	Control	D/C/F/TAF	Control	D/C/F/TAF	Control
n	763	378	507	252	256	126	623	313	140	65	597	293	155	82
≥1 AE	82	82	82	82	81	83	82	83	82	79	83	82	77	82
Discontinued due to an AE	1	1	1	<1	2	3	2	2	1	0	1	2	2	0
≥1 grade 3-4 AE	7	8	6	8	8	9	7	8	7	8	8	9	4	6
≥1 serious AE	5	5	4	4	6	7	5	5	3	6	5	4	3	6

Table 3. Incidence (%) of Bone AEs of Interest Through Week 48

	Overall population		Age subgroups				Gender subgroups				Race subgroups			
			≤50 years		>50 years		Men		Women		Non-black/ African American		Black/ African American	
Parameter, %	D/C/F/TAF	Control	D/C/F/TAF	Control	D/C/F/TAF	Control	D/C/F/TAF	Control	D/C/F/TAF	Control	D/C/F/TAF	Control	D/C/F/TAF	Control
n	763	378	507	252	256	126	623	313	140	65	597	293	155	82
Bone loss/atrophy	6	7	7	7	6	6	7	6	4	8	8	7	2	4
Related	1	3	1	2	1	3	1	3	1	2	1	3	0	1
Fracture, other	1	1	1	<1	2	1	1	1	1	0	1	1	1	0
Related	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other bone events	<1	1	<1	1	1	0	1	<1	0	2	1	1	0	0
Related	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Figure 5. Mean percentage change in BMD from baseline to Week 48.*



*Data are from the bone investigation substudy, which included 204 patients in the D/C/F/TAF arm and 104 patients in the control arm.

CONCLUSIONS

- **Low rates of virologic rebound, as well as improved renal function and bone safety, were observed regardless of age, gender, or race in virologically suppressed, HIV-1–infected adults, including those with prior VF, who switched from bPI + FTC/TDF to D/C/F/TAF compared with control**
  - **A limitation of the analyses was the small numbers of patients in the subgroups (eg, >50 years, women, black/African American)**
- **Patients who switched to D/C/F/TAF had low, noninferior cumulative virologic rebound rates through Week 48 (2.5%) versus control (2.1%), and no resistance to study drugs was observed**

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DISCLOSURES

G.D. Huhn, E. DeJesus, and P.-M. Girard contributed to the conduct of the study as investigators and to the interpretation of the data. R. Petrovic contributed to statistical analysis and interpretation of the data. E.Y. Wong and K. Brown contributed to the design of the study and interpretation of the data. All authors contributed to drafting the poster and approved the final version.

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