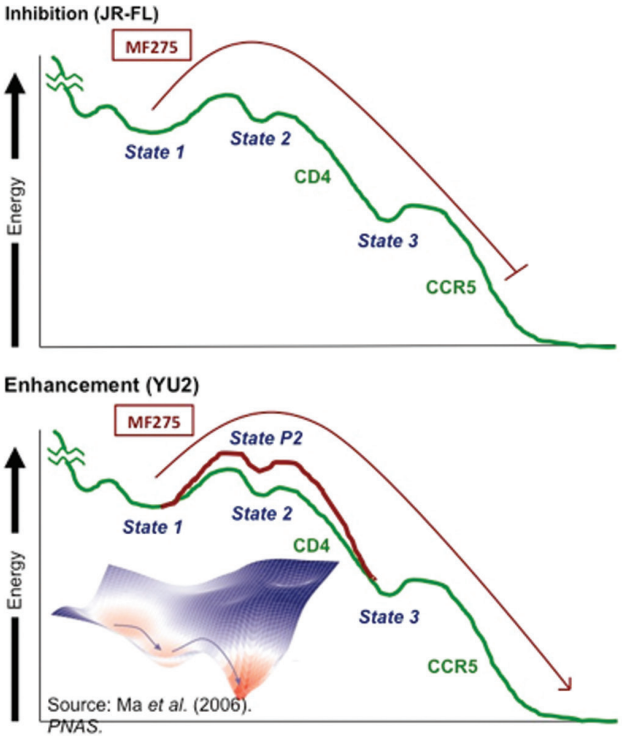

Figure 2. Proposed mechanisms for MF275 inhibition and activation. In Envs with baseline conformations more prone to inhibition (e.g. JR-FL), MF275 triggers transition from State 1 to States 2 and 3. Upon CCR5 binding, however, MF275 acts as a steric blockade to 6HB formation, removable with washout. In Envs more prone to activation (e.g. YU2), MF275 triggers transition from State 1 to States P2 and 3, which are parallel to but conformationally distinct from those induced by CD4 or CD4-mimetics. These activated intermediates are metastable, even with washout of MF275, and can mediate CD4-independent infection in the presence of CCR5.

Disclosures. **All authors:** No reported disclosures.

541. Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide in HIV-1 Treatment Naïve Patients: Week 48 Results in Subgroups Based on Baseline Viral Load, CD4$^+$ Count, and WHO Clinical Staging

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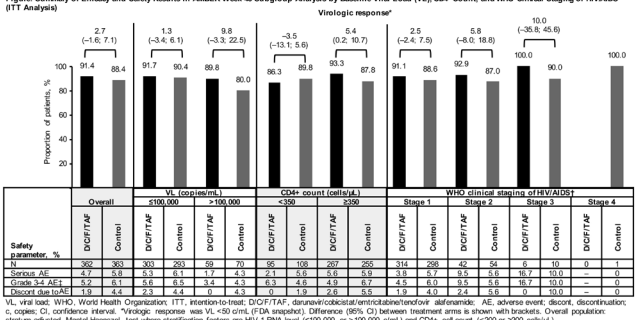
Background. Darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) 800/150/200/10 mg is a once-daily, single-tablet regimen approved in Europe and under regulatory review in the United States for the treatment of HIV-1 infection. In the pivotal AMBER trial in antiretroviral treatment (ART)-naïve, HIV-1–infected adults, D/C/F/TAF achieved a high virologic response rate at Week 48 that was non-inferior to control (D/C+F/tenofovir disoproxil fumarate); favorable renal/bone outcomes were seen with D/C/F/TAF vs. control. These results were consistent across age, gender, and race subgroups. Here we report Week 48 results in subgroups based on viral load (VL), CD4$^+$ count, and WHO clinical staging of HIV/AIDS at baseline.

Methods. The phase 3, randomized (1:1), blinded, noninferiority AMBER trial enrolled ART-naïve, HIV-1–infected adults. The primary endpoint was the proportion of patients with virologic response (VL <50 copies/mL; FDA snapshot) at Week 48. Adverse events (AEs) and laboratory parameters were monitored throughout the study. Results were evaluated in subgroups based on VL (≤ vs. >100,000 copies/mL), CD4$^+$ count (< vs. ≥350 cells/μL), and WHO clinical stage (1 vs. 2 vs. 3 vs. 4) at baseline.

Results. Of the 725 patients randomized and treated, the majority had VL ≤100,000 copies/mL (82% of patients), CD4$^+$ count ≥350 cells/μL (72%), and WHO clinical stage 1 (84%) at baseline. Overall virologic response rates were 91.4% with D/C/F/TAF and 88.4% with control; results were similar across baseline VL, CD4$^+$ count, and WHO clinical stage subgroups (figure). Overall rates of serious AEs, grade 3–4 AEs, and AE-related discontinuations were similar for D/C/F/TAF (n = 17 [4.7%], n = 19 [5.2%], and n = 7 [1.9%], respectively) and control (n = 21 [5.8%], n = 22 [6.1%], and n = 16 [4.4%]), as well as across subgroups (table).

Conclusion. D/C/F/TAF achieved high (91.4%), noninferior virologic response rates vs. control (88.4%) in ART-naïve, HIV-1–infected adults. Consistent and robust efficacy and safety results were found with D/C/F/TAF vs. control based on VL, CD4$^+$ count, and WHO clinical stage at baseline.

Figure. Summary of Efficacy and Safety Results in AMBER Week 48 Subgroup Analysis by Baseline Viral Load (VL), CD4$^+$ Count, and WHO Clinical Staging of HIV/AIDS (ITT Analysis)



Safety parameter, %	Overall		VL (copies/mL) ≤100,000		VL (copies/mL) >100,000		CD4+ count (cells/μL) <350		CD4+ count (cells/μL) ≥350		WHO clinical staging of HIV/AIDS† Stage 1		Stage 2		Stage 3		Stage 4	
	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	D/C/F/TAF	Control	D/C/F/TAF	Control
N	362	363	303	293	59	70	95	108	267	255	314	298	42	54	6	10	0	1
Serious AE	4.7	5.8	5.3	6.1	1.7	4.3	2.1	5.6	5.6	5.9	3.8	5.7	9.5	5.6	16.7	10.0	–	0
Grade 3-4 AE‡	5.2	6.1	5.6	6.5	3.4	4.3	6.3	4.6	4.9	6.7	4.5	6.0	9.5	5.6	16.7	10.0	–	0
Discont due to AE	1.9	4.4	2.3	4.4	0	4.3	0	1.9	2.6	5.5	1.9	4.0	2.4	5.6	0	10.0	–	0

VL, viral load; WHO, World Health Organization; ITT, intention-to-treat; D/C/F/TAF, darunavir/cobicistat/emtricitabine/tenofovir alafenamide; AE, adverse event; discont, discontinuation; c, copies; CI, confidence interval. *Virologic response was VL <50 c/mL (FDA snapshot). Difference (95% CI) between treatment arms is shown with brackets. Overall population: stratum-adjusted Mantel-Haenszel test where stratification factors are HIV-1 RNA level (≤100,000 or >100,000 c/mL) and CD4+ cell count (<200 or ≥200 cells/μL). †Stage 1 = asymptomatic, stage 2 = mild symptoms, stage 3 = advanced symptoms, stage 4 = severe symptoms. ‡With ≥1 worst grade 3-4 AE.

Disclosures. **B. Rashbaum**, Gilead: Shareholder and Speaker's Bureau: Any financial benefit related to being a shareholder and Speaker honorarium. **C. Mcdonald**, Gilead: Various, Personal fees. Merck: Various, Personal fees. ViiV: Various, Personal fees. Janssen: Various, Personal fees. **D. Luo**, Janssen: Employee, Salary. **J. Jezorwski**, Janssen: Employee, Salary. **K. Brown**, Janssen: Employee, Salary. **E. Y. Wong**, Janssen: Employee, Salary.

This abstract has been withdrawn at the author's request.

543. An Integrated Safety Analysis Comparing Once-Daily Doravirine (DOR) to Darunavir+Ritonavir (DRV+r) and Efavirenz (EFV) in HIV-1-Infected, Antiretroviral Therapy (ART)-Naïve Adults

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