LATE BREAKER ABSTRACT

LB1. Doravirine/Lamivudine/Tenofovir DF Continues to Be NonInferior to Efavirenz/Emtricitabine/Tenofovir DF in Treatment-Naïve Adults With HIV-1 Infection: Week 96 Results of the DRIVE-AHEAD Trial

Chloe Orkin, MBBCh[1]; Kathleen Squires, MD[2]; Jean-Michel Molina, MD[3]; Paul Sax, MD[4]; Wingwai Wong, MD[5]; Otto Sussmann, MD[6]; Gina Lin, MS[7]; Sushma Kumar, PhD[7]; George Hanna, MD[7]; Carey Hwang, MD, PhD[7]; Elizabeth Martin, DO, MPH[7] and Hedy Teppler, MD[8], [1]Department of Infection and Immunity, Royal London Hospital and Queen Mary University, Barts Health NHS Trust, London, UK, [2]Sidney Kimmel Medical College of Thomas Jefferson University Philadelphia, Philadelphia, Pennsylvania, [3]Department of Infectious Diseases, University of Paris Diderot, Sorbonne Paris Cité; Hôpital Saint-Louis, Assistance Publique-Hôpitaux de Paris, Paris, France, [4]Brigham and Women's Hospital, Boston, Massachusetts, [5]Taipei Veterans General Hospital, Taipei, Taiwan, [6]Infectious Diseases, Hospital San Rafael De Tunja, Tunja, Colombia, [7]Merck & Co., Inc., Kenilworth, New Jersey, [8]Merck, Upper Gwynedd, Pennsylvania

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Background. Doravirine (DOR) is a novel non-nucleoside reverse-transcriptase inhibitor (NNRTI). In the phase 3 DRIVE-AHEAD trial in HIV-1-infected treatment-naïve adults, DOR demonstrated noninferior efficacy to efavirenz (EFV) and favorable profiles for neuropsychiatric tolerability and lipids at 48 weeks. We present data through week 96.

Methods. DRIVE- AHEAD (Clinical Trials Registration: NCT02403674) is a phase 3, multicenter, double-blind, noninferiority trial that compared DOR with EFV. Eligible participants were HIV-1-infected treatment-naïve adults with pre-treatment HIV-1 RNA ≥1,000 copies/mL. Participants were randomized (1:1) to a fixed-dose regimen of DOR 100 mg, lamivudine 300 mg and tenofovir disoproxil fumarate 300 mg (DOR/3TC/TDF) QD or EFV 600 mg, emtricitabine 200 mg and TDF 300 mg (EFV/FTC/TDF) QD for up to 96 weeks. Randomization was stratified by screening HIV-1 RNA (≤/>100,000 copies/mL) and hepatitis B/C co-infection (yes/no). The efficacy endpoint of interest at week 96 was HIV-1 RNA <50 copies/mL with predefined noninferiority margin of 10%. Safety endpoints of interest included occurrence of pre-specified neuropsychiatric adverse events and mean change from baseline in fasting lipid levels at week 96.

Results. Of 734 participants randomized, 728 received study drug and were included in analyses (mean age 33 years, 85% male, 48% white, 19% black, 34% Hispanic). At week 96, HIV-1 RNA <50 copies/mL was achieved by 77.5% of DOR/3TC/TDF recipients vs. 73.6% of EFV/FTC/TDF recipients (difference 3.8%, 95%CI [−2.4, 10.0]). No additional phenotypic resistance to DOR was observed between weeks 48 and 96, while two additional participants in the EFV/FTC/TDF group developed resistance to EFV. Dizziness, sleep disorders/disturbances, altered sensorium, and rash were less frequent in DOR/3TC/TDF recipients than in EFV/FTC/TDF recipients. Fasting LDL-C and non-HDL-C increased in the EFV/FTC/TDF group but not in the DOR/3TC/TDF group, while change in total cholesterol/HDL-C ratio was similar.

Conclusion. Week 96 results support non-inferiority of DOR/3TC/TFD to EFV/FTC/TDF established at Week 48 with no additional DOR resistance between week 48 and 96. DOR/3TC/TDF was safe and well-tolerated with fewer neuropsychiatric and rash events and favorable lipid profile compared with EFV/FTC/TDF.

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Week 96 Efficacy & Safety Outcomes

HIV-1 RNA <50 copies/mL	DOR/3TC/TDF n/N	%	EFV/FTC/TDF n/N	%	Difference % (95% CI)
Overall†	282/364	77.5	268/364	73.6	3.8 (-2.4, 10.0)
Baseline HIV-1 RNA ≤100,000‡	233/268	86.9	217/248	87.5	-0.6 (-6.4, 5.3)
Baseline HIV-1 RNA >100,000‡	49/69	71.0	51/64	79.7	-8.1 (-22.9, 6.7)
Baseline CD4+ T-cell count ≤200 cells/mm³‡	26/40	65.0	32/39	82.1	-16.9 (-36.9, 3.0)
Baseline CD4+ T-cell count >200 cells/mm³‡	256/297	86.2	236/273	86.4	-0.3 (-5.9, 5.4)
Phenotypic resistance*	6/364	1.6	13/364	3.6	NA

Adverse Event (AE) Summary	DOR/3TC/TDF (N=364)	EFV/FTC/TDF (N=364)	Difference % (95% CI)
One or more AE	88.2 %	93.1 %	-4.9 (-9.3, -0.7)
Drug-related AE	31.9 %	64.8 %	-33.0 (-39.6, -26.0)
Serious AE	5.8 %	8.2 %	-2.5 (-6.3, 1.3)
Discontinued due to AE	3.0 %	7.4 %	-4.4 (-7.9, -1.2)
Dizziness	10.2 %	38.2 %	-28.0 (-33.9, -22.1)
Sleep disorders/disturbances	14.0 %	27.5 %	-13.5 (-19.3, -7.6)
Altered sensorium	4.9 %	8.5 %	-3.6 (-7.4, 0.1)
Rash	5.5%	12.4%	-6.9 (-11.2, -2.8)

Fasting Lipids, Change from BL	N	Mean Δ	N	Mean Δ	Difference (95% CI)
LDL cholesterol (mg/dL)	330	-0.62	306	10.78	-11.1 (-14.8, -7.4)
Non-HDL cholesterol (mg/dL)	333	-2.14	315	14.95	-17.0 (-21.1, -13.0)
Total cholesterol to HDL-C Ratio	333	-0.12	315	-0.10	-0.04 (-0.23, 0.15)

† FDA Snapshot method; 95% CI for treatment difference based on stratum-adjusted Mantel-Haenszel method. Non-inferiority bound pre-specified as -10 percentage points.
‡ Observed Failure (OF) approach for missing data.
*Phenotypic resistance- number of participants with protocol defined virologic failure and participants who discontinued early that developed phenotypic resistance to DOR or EFV, respectively.

LB2. Switch to Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate (DOR/3TC/TDF) Maintains Virologic Suppression Through 48 Weeks: Results of the DRIVE-SHIFT Trial

Princy Kumar, M.D.[1]; Margaret Johnson, MD, FRCP[2]; Jean-Michel Molina, MD[3]; Giuliano Rizzardini, MD[4]; Pedro Cahn, MD, PhD[5]; Markus Bickel, MD[6]; Josep Mallolas, MD[7]; Yan Zhou, PhD[8]; Cristiana Morais, PhD[8]; Sushma Kumar, PhD[8]; Peter Sklar, MD, MPH[8]; George J. Hanna, MD[8]; Carey Hwang, MD, PhD[8] and Wayne Greaves, MD[8], [1]Division of Infectious Diseases and Travel Medicine, Medstar Georgetown University Hospital, Washington, DC, [2]Royal Free Hospital, London, UK, [3]University of Paris Diderot and Hôpital Saint-Louis, Paris, France, [4]ASST Fatebenefratelli Sacco, Milan, Italy, [5]Fundación Huésped, Buenos Aires, Argentina, [6]Infektiologikum, Frankfurt, Germany, [7]University of Barcelona, Barcelona, Spain, [8]Merck & Co., Inc., Kenilworth, New Jersey

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Background. Doravirine is a novel, non-nucleoside reverse-transcriptase inhibitor (NNRTI) that has demonstrated efficacy in two Phase 3 trials in treatment-naïve adults with HIV-1.

Methods. This open-label, active-controlled, noninferiority (NI) trial evaluated a once-daily single-tablet regimen of doravirine 100 mg, lamivudine 300 mg, and tenofovir disoproxil fumarate 300 mg (DOR/3TC/TDF) vs. continuation of current therapy in adults with HIV-1 virologically suppressed for ≥6 months on a stable regimen of two NRTIs plus a boosted protease inhibitor (PI), boosted elvitegravir, or NNRTI. Participants with screening HIV-1 RNA <40 copies/mL, no history of virologic failure on any regimen, and no resistance to DOR/3TC/TDF were randomized (2:1) to start DOR/3TC/TDF on Day 1 (immediate switch group, ISG) or after 24 weeks (delayed switch group, DSG). The primary endpoint was the proportion (%) of participants with HIV-1 RNA <50 copies/mL (FDA snapshot approach), with the primary comparison between ISG at Week 48 and DSG at Week 24 and a secondary comparison between the groups at Week 24; the NI margin was -8%. The % of participants with HIV-1 RNA ≥50 copies/mL was also analyzed (FDA snapshot approach; NI margin 4%).

Results. A total of 670 participants (447 ISG, 223 DSG) were treated and included in the analyses; 84.5% were male, 76.4% were white, and mean age was 43.3 years. At Week 24, 93.7% (419/447) of ISG vs. 94.6% (211/223) of DSG had HIV-1 RNA <50 copies/mL (difference −0.9% [−4.7, 3.0]), and 1.8% of each group had HIV-1 RNA ≥50 copies/mL. At Week 48, 90.8% (406/447) of ISG maintained HIV-1 RNA <50 copies/mL (vs. 94.6% of DSG at Week 24; difference −3.8%, 95% CI [−7.9%, 0.3%]), and 1.6% of ISG had HIV-1 RNA ≥50 copies/mL. In the ritonavir-boosted PI stratum, mean changes in fasting LDL-C and non-HDL-C at Week 24 were significantly lower ($P < 0.0001$) in ISG vs. DSG (table). Rates of any AE and of drug-related AEs at Week 24 were higher in ISG vs. DSG. AEs were mild in most ISG participants (64% of those with any AE; 80% of those with drug-related AEs).

Conclusion. A once-daily single-tablet regimen of DOR/3TC/TDF demonstrated non-inferior efficacy and acceptable safety compared with continuing therapy, and is an option for maintaining viral suppression in patients considering a change in therapy.

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