PIFELTRO™ (doravirine): Efficacy and Weight Change Data in HIV-1 Patients

PIFELTRO is indicated in combination with other antiretroviral (ARV) agents for the treatment of HIV-1 infection in adult patients with no prior ARV treatment history or to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable ARV regimen with no history of treatment failure and no known substitutions associated with resistance to doravirine.

Primary efficacy outcome: Proportion of patients with HIV-1 ≥50 copies/mL: 2% for a doravirine-based FDC (ISG at week 48) vs 1% for baseline regimen (DSG at week 24). Difference (95% CI): 0.7 (-1.3, 2.6)

DRIVE-SHIFT Study Design: A randomized, international, multicenter, open-label study of adults with virologically suppressed HIV-1 for ≥6 months on 2 NRTIs with a PI plus either ritonavir or cobicistat, or elvitegravir plus cobicistat, or an NNRTI, with no history of virologic failure. Patients either immediately switched to a doravirine-based FDC on Day 1 of the study for 48 weeks (ISG [n=447]) or continued on their baseline regimen and switched after 24 weeks to a doravirine-based FDC (DSG [n=223]).

Weight Change in Virologically Suppressed Adults

Change in body weight from baseline (kg) through week 48[1,a]

Doravirine-based FDC Immediate Switch Group (weeks 0-48)			Baseline Regimen Delayed Switch Group (weeks 0-24)			Doravirine-based FDC Delayed Switch Group (weeks 24-48)		
n	Mean Change (95% CI)	Median Change (Q1, Q3)	n	Mean Change (95% CI)	Median Change (Q1, Q3)	n	Mean Change (95% CI)	Median Change (Q1, Q3)
408	0.74 kg (0.4, 1.1)	0.6 kg (-1.3, 2.9)	214	-0.32 kg (-0.80, 0.16)	0.0 kg (-1.55, 1.20)	202	0.55 kg (0.1, 1.0)	0.2 kg (-1.0, 2.0)

The mean and median changes were a retrospective data analysis. The data were from a clinical study of virologically suppressed adults.

Because mean and median changes from baseline in weight were not pre-specified, and because other data related to weight gain were not measured, comparisons between treatment arms of individual trials should not be made. These results should be interpreted with caution.

[a] Baseline regimen = PI plus either ritonavir or cobicistat, or elvitegravir plus cobicistat, or an NNRTI, each administered with 2 NRTIs.

SELECTED SAFETY INFORMATION

- PIFELTRO is contraindicated when co-administered with drugs that are strong cytochrome P450 (CYP)3A enzyme inducers (including the anticonvulsants carbamazepine, oxcarbazepine, phenobarbital, and phenytoin; the androgen receptor inhibitor enzalutamide; the antimycobacterials rifampin and rifapentine; the cytotoxic agent mitotane; and the herbal product St. John's wort (*Hypericum perforatum*)), as significant decreases in PIFELTRO plasma concentrations may occur, which may decrease the effectiveness of PIFELTRO.
- Immune reconstitution syndrome can occur, including the occurrence of autoimmune disorders with variable time to onset, which may necessitate further evaluation and treatment.
- Co-administration of PIFELTRO with efavirenz, etravirine, or nevirapine is not recommended.
- If co-administered with rifabutin, increase PIFELTRO dosage to one tablet twice daily (approximately 12 hours apart).
- Consult the full Prescribing Information prior to and during treatment for more information on potential drug-drug interactions.
- The most common adverse reactions with PIFELTRO (incidence ≥5%, all intensities) were nausea (7%), dizziness (7%), headache (6%), fatigue (6%), diarrhea (6%), abdominal pain (5%), and abnormal dreams (5%).
- By Week 96 in DRIVE-FORWARD, 2% of adult subjects in the PIFELTRO group and 3% in the DRV+r group had adverse events leading to discontinuation of study medication.
- By Week 96 in DRIVE-AHEAD, 3% of adult subjects in the DELSTRIGO™ (doravirine/3TC/TDF) group and 7% in the EFV/FTC/TDF group had adverse events leading to discontinuation of study medication.
- In DRIVE-FORWARD, mean changes from baseline at Week 48 in LDL-cholesterol (LDL-C) and non-HDL-cholesterol (non-HDL-C) were pre-specified. LDL-C: -4.6 mg/dL in the PIFELTRO group vs 9.5 mg/dL in the DRV+r group. Non-HDL-C: -5.4 mg/dL in the PIFELTRO group vs 13.7 mg/dL in the DRV+r group. The clinical benefits of these findings have not been demonstrated.
- In DRIVE-AHEAD, mean changes from baseline at Week 48 in LDL-C and non-HDL-C were pre-specified. LDL-C: -2.1 mg/dL in the DELSTRIGO group vs 8.3 mg/dL in the EFV/FTC/TDF group. Non-HDL-C: -4.1 mg/dL in the DELSTRIGO group vs 12.7 mg/dL in the EFV/FTC/TDF group. The clinical benefits of these findings have not been demonstrated.
- In DRIVE-SHIFT, mean changes from baseline at Week 48 in LDL-C and non-HDL-C were pre-specified. LDL-C: -16.3 mg/dL in the DELSTRIGO group vs -2.6 mg/dL in the PI + ritonavir group. Non-HDL-C: -24.8 mg/dL in the DELSTRIGO group vs -2.1 mg/dL in the PI + ritonavir group. The clinical benefits of these findings have not been demonstrated.

Selected Safety Information continued on next page.

Pifeltro™
doravirine
100 mg tablets

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SELECTED SAFETY INFORMATION *(continued)*

- In DRIVE-AHEAD, neuropsychiatric adverse events were reported in the three pre-specified categories of sleep disorders and disturbances, dizziness, and altered sensorium. Twelve percent of adult subjects in the DELSTRIGO group and 26% in the EFV/FTC/TDF group reported neuropsychiatric adverse events of sleep disorders and disturbances; 9% in the DELSTRIGO group and 37% in the EFV/FTC/TDF group reported dizziness; and 4% in the DELSTRIGO group and 8% in the EFV/FTC/TDF group reported altered sensorium.
- The safety of DELSTRIGO in virologically-suppressed adults was based on Week 48 data from subjects in the DRIVE-SHIFT trial. Overall, the safety profile in virologically-suppressed adult subjects was similar to that in subjects with no ARV treatment history.
- There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to PIFELTRO during pregnancy. Healthcare providers are encouraged to register patients by calling the Antiretroviral Pregnancy Registry (APR) at 1-800-258-4263.
- Mothers infected with HIV-1 should be instructed not to breastfeed if they are receiving PIFELTRO due to the potential for HIV-1 transmission.

Before prescribing PIFELTRO™ (doravirine), please read the accompanying Prescribing Information. The Patient Information also is available.

3TC, lamivudine; DRV+r, darunavir+ritonavir; EFV, efavirenz; FTC, emtricitabine; HIV-1, human immunodeficiency virus type 1; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; RNA, ribonucleic acid; TDF, tenofovir disoproxil fumarate.

Reference:
1. Data available on request from Merck Professional Services-DAP, WP1, PO Box 4, West Point, PA 19486-0004. Please specify information package US-DOV-00353.

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