Commonly used non-nucleoside reverse transcriptase inhibitors (NNRTIs) are associated with suboptimal efficacy and/or safety profiles. For instance, efavirenz (EFV) is often recommended as a first-line therapy for HIV infection in resource-poor settings, but its use is limited by suboptimal efficacy and frequent drug-related adverse events (AEs). In particular, drug-related AEs were significantly less common in the DOR 100 mg group compared to the EFV 600 mg group. DOR was associated with similar to efavirenz (EFV) with TDF/FTC at Week 24, as demonstrated by the Phase 2 study (MK-1439 Protocol 007). EFV 600 mg: Part 1 (n=43) + Part 2 (n=66); total=109 patients. DOR 100 mg: Part 1 (n=42) + Part 2 (n=66); total=108 patients. DOR 25, 50, 100, and 200 mg QD with TDF/FTC was associated with similar virologic activity and immunological effects compared to EFV 600 mg with TDF/FTC at Week 24 in this study. DOR 200 mg was selected for Part 1 for evaluation in the Phase 3 program.

**Background**

Antiretroviral activity of DOR 25, 50, 100, and 200 mg QD with TDF/FTC was associated with similar virologic activity and immunological effects compared to EFV 600 mg with TDF/FTC at Week 24 in this study. DOR 200 mg was selected for Part 1 for evaluation in the Phase 3 program.

**Results**

**Virologic response:** Proportion of patients with HIV RNA <40 copies/mL (primary), with HIV RNA <40 copies/mL at the time of virologic failure. Another patient who failed on DOR had a sample tested for resistance 1 month after initial failure. The failure was noted during therapy and viral load increased. This patient was subsequently placed on atazanavir/ritonavir and remained suppressed for the duration of the study.

**Success (HIV RNA <40 copies/mL) at Week 48**

- **DOR 100 mg (N=108)**: 92/108 (85.2%)
- **EFV 600 mg (N=109)**: 92/109 (84.4%)

**Conclusions**

In ART-naive subjects with HIV-1 infection, doravirine 100 mg QD in combination with TDF/FTC:
- Demonstrates antiretroviral activity and immunological effect similar to efavirenz with TDF/FTC at Week 48.
- Is safe and generally well tolerated through Week 48.
- Drug-related AEs were significantly less common in the DOR group (81.5%) vs the EFV group (95.6%).

Phase 3 trials of doravirine 100 mg QD are currently ongoing.

**Clinical Outcomes**

**Summary of Week 48 Outcomes**

- **Success (HIV RNA <40 copies/mL) at Week 48**
  - **DOR 100 mg (N=108)**: 92/108 (85.2%)
  - **EFV 600 mg (N=109)**: 92/109 (84.4%)

**Additional studies**

- **DOR 25 mg**
  - **Success (HIV RNA <40 copies/mL) at Week 48**
    - **DOR 25 mg (N=132)**: 115/132 (87.1%)

**Safety endpoints**

- **Drug-related AEs** were significantly less common in the DOR 100 mg group compared to the EFV 600 mg group. DOR was associated with similar to efavirenz (EFV) with TDF/FTC at Week 24, as demonstrated by the Phase 2 study (MK-1439 Protocol 007). EFV 600 mg: Part 1 (n=43) + Part 2 (n=66); total=109 patients. DOR 100 mg: Part 1 (n=42) + Part 2 (n=66); total=108 patients. DOR 25, 50, 100, and 200 mg QD with TDF/FTC was associated with similar virologic activity and immunological effects compared to EFV 600 mg with TDF/FTC at Week 24 in this study. DOR 200 mg was selected for Part 1 for evaluation in the Phase 3 program.

**References**


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