Proprietary

Five-Year Effectiveness of Doravirine-Based ART in Treatment-Experienced People Living With HIV

Vincent Lanting,[1] Daoud Ait Moha,[1] Sean Fleming,[2] Anouk Schaeffers,[3] Girish Prajapati,[2] Floris Vuijk,[3] Kees Brinkman[1]
[1]Department of Internal Medicine, OLVG, Amsterdam, the Netherlands, [2]Merck & Co., Inc., Rahway, NJ, USA, [3]MSD B.V., Haarlem, the Netherlands

538

BACKGROUND

Doravirine (DOR) is a non-nucleoside reverse transcriptase inhibitor (NNRTI) used in treatment- experienced and naïve people living with HIV (PLWH). This study evaluated the long-term effectiveness of DOR-based ART among PLWH who were virologically suppressed (VS) prior to switching to a DOR-based regimen.

METHODS

- Retrospective cohort with all VS PLWH ≥18 years switched to DOR/3TC/TDF or DOR + ≥1 NRTI and/or 1 INSTI between September 2019 and February 2024.
- VS defined as HIV RNA viral load (VL) <50 copies/mL.
- Exclusion criteria included pregnancy, ART regimens likely indicating intensification or highly treatment experienced PLWH, end-stage renal disease, and primary or secondary DOR resistance mutations.
- Primary outcome: Proportion of PLWH maintaining VS at 5 years.
- Secondary outcomes: Proportion of PLWH maintaining VS at 1, 2, 3, and 4 years; immunologic effectiveness.
  - VL measures taken ±90 days of the respective time point were included for all VS outcomes
- Reasons for discontinuation included:
  - Virologic failure (VF), defined as two consecutive VL >200 copies/mL or 1 VL >200 copies/mL and DOR discontinuation.
  - Toxicities defined in the medical chart, including medical reasons and PLWH-reported adverse effects.
- PLWH were censored if they switched to another ART regimen, died, were lost to follow-up (no observations ≥10 months after the last prescription), or study end of March 31, 2025.

Abbreviations:
3TC: lamivudine; ART: antiretroviral therapy; BIC: bictegravir; c: cobicistat; DOR: doravirine; BMI: Body mass index; DTG: dolutegravir; EVG: elvitegravir; FTC: emtricitabine; HIV: human immunodeficiency virus; INSTI: integrase strand transfer inhibitor; IQR: interquartile range; NNRTI: non-nucleoside reverse transcriptase inhibitor; NRTI: nucleoside reverse transcriptase inhibitor; PLWH: people living with HIV; RPV: rilpivirine; SD: standard deviation; TAF: tenofovir alafenamide; TDF: tenofovir disoproxil fumarate; VF: virologic failure; VL: viral load; VS: virologically suppressed.

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Doravirine-based regimens maintained a high rate of virologic suppression in people living with HIV. These results suggest long-term effectiveness of doravirine in treatment experienced PLWH with up to 5 years follow-up.

RESULTS

Of 1,126 PLWH switched to a DOR-based regimen, 1,052 were included in the analysis with a median follow-up of 43 months (interquartile range [IQR] 19-59). Over the entire study period, 10 (1.0%) PLWH died and 84 (8.0%) were lost to follow-up.

Table 1. Baseline characteristics

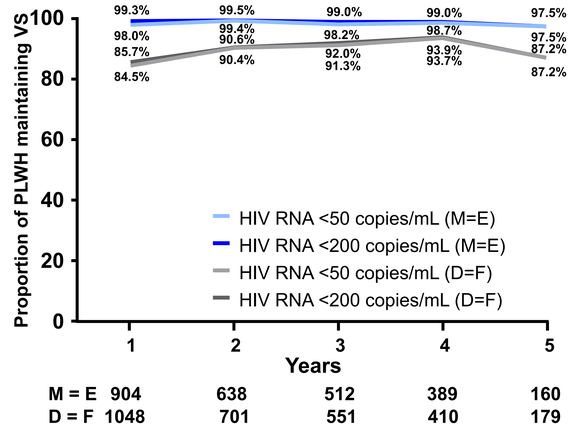
Baseline characteristics	N=1,052
Age in years, median (IQR)	50 (41-58)
Sex, male, n (%)	958 (91.0%)
Years since HIV diagnosis, median (IQR)	11 (7-17)
Prior ART: EVG/c/FTC/(TAF or TDF), n (%)	272 (25.9%)
Prior ART: RPV/FTC/(TAF or TDF), n (%)	227 (21.6%)
Prior ART: BIC/FTC/TAF, n (%)	142 (13.5%)
Prior ART: DTG + FTC/(TAF or TDF), n (%)	119 (11.3%)
Prior ART: Other, n (%)	292 (27.8%)
Baseline ART: DOR/3TC/TDF, n (%)	1,034 (98.3%)
Baseline ART: DOR + ≥1 NRTI and/or 1 INSTI, n (%)	18 (1.7%)
BMI mean (SD)	25.7 (4.4)

Table 2. Discontinuation of DOR during follow-up

Follow-up	Year 1	Year 2	Year 3	Year 4	Year 5
Stopped, n (%)	148 (14.1)	68 (8.2)	39 (5.9)	22 (4.5)	19 (8.6)
Virologic failure	4 (0.4)	5 (0.6)	0	1 (0.2)	0
Medical reason	21 (2.0)	23 (2.8)	16 (2.4)	7 (1.4)	10 (4.5)
PLWH-reported adverse effect	107 (10.2)	26 (3.2)	12 (1.8)	7 (1.4)	5 (2.3)
Other	16 (1.5)	14 (1.7)	11 (1.7)	7 (1.4)	4 (1.8)

- 5/10 PLWH with VF had historical resistance testing with no resistance to DOR, 3TC, or TDF
  - 6/10 developed resistance to DOR (6/6), 3TC (4/6), or TDF (2/6)
    - 1 re-suppressed on DRV/c + DTG; 1 on DRV/c/FTC/TAF + bid DTG; 4 on BIC/FTC/TAF
  - 2/10 had no resistance detected
    - 2 re-suppressed on BIC/FTC/TAF; 1 after no VS on DRV/c/FTC/TAF
  - 2/10 had viral loads too low for testing
    - 1 re-suppressed on BIC/FTC/TAF + DRV/c; 1 on DOR/3TC/TDF after VF on BIC/FTC/TAF

Figure 1. Virologic Effectiveness on DOR-based regimens



[1]M = E: Missing = Excluded; [2]D = F: Discontinuation = Failure

[1]PLWH with a viral load measure and have continued DOR treatment up to the respective time point
[2]PLWH switched to DOR-based ART including those who discontinued or were lost to follow-up who were treated as "failure" (not having a viral load below the defined threshold)

Table 3. Immunologic Effectiveness on DOR-based regimens

Parameter	Year 1	Year 2	Year 3	Year 4	Year 5
Number of PLWH (baseline + follow-up measure)	448	321	219	142	46
CD4 T-cell count, median (IQR)	760 (580—947)	784 (587—990)	802 (639—1053)	830 (627—1047)	806 (653—992)
Difference compared with baseline, median (IQR)	-4 (109—99)	31 (-104—149)	76 (-75—198)	75 (-53—240)	105 (-8—274)

CONCLUSIONS

The rate of virologic suppression remained high and the occurrence of virologic failure was rare among PLWH over 5 years of follow-up on DOR-based regimens. These results support the long-term effectiveness of DOR in treatment-experienced people living with HIV.

PLAIN LANGUAGE SUMMARY

Among PLWH with up to 5 years of follow-up, doravirine-based ART maintained virologic suppression in most PLWH, with few cases of treatment failure, and modest numbers of discontinuations. Doravirine was effective over the long-term in treatment experienced PLWH.

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