Weight Change After Starting Doravirine among ART-Experienced Individuals in the US

Poster 807

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Background

- Doravirine (DOR) is a third generation NNRTI approved by the FDA on 30AUG2018.
- Integrase inhibitors (INSTI) and tenofovir alafenamide (TAF) have been associated with weight gain.[1]
- Efavirenz (EFV) and tenofovir disoproxil fumarate (TDF) have been associated with weight loss.[1]
- The impact on weight of other non-nucleoside reverse transcriptase inhibitors (NNRTI) such as DOR is unclear.

Objective

To assess changes in weight over time after starting DOR among virologically suppressed individuals.

Methods

Study population

- OPERA cohort: prospectively captured, routine clinical data from electronic health records in the US (101 clinics, 23 US states/territories), representing ~15% of people with HIV in the US.
- Inclusion criteria
  - ART-experienced people with HIV-1
  - Switch to DOR-containing regimen between 30AUG2018 and 31DEC2022
  - Viral load <50 copies/mL at switch
  - ≥1 weight measurement within 6 months before switch and ≥1 follow-up weight measurement
- Censored at the 1st of: (a) DOR discontinuation, (b) >45 days without ART, (c) 12 months after last clinical contact, (d) death, or (e) study end (31MAY2023)

Statistical analyses

- Changes in weight (kg) over time on DOR: univariate linear mixed model with random intercept
  - Patterns of change: restricted cubic splines on time
  - Rate of change: no splines
  - Overall and stratified by sex
- Sensitivity analyses accounting for patterns of use of other antiretrovirals (ARV):
  1. Stratification by EFV and/or TDF use before/after switch
  2. Population restricted to those who maintained the same INSTI/TAF combination before and after switch (first 36 months)

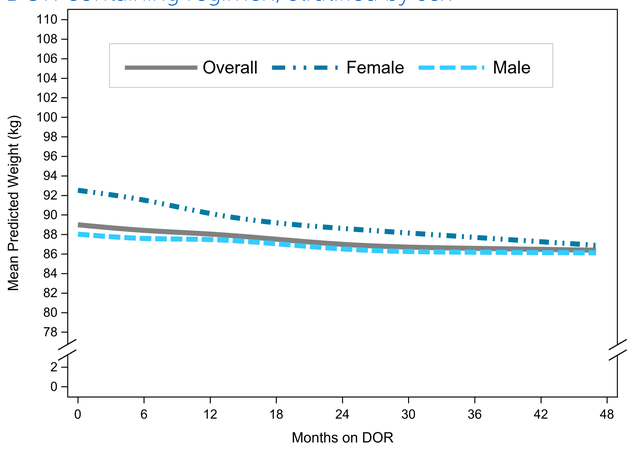
Results

Table 1. Baseline characteristics of virologically suppressed individuals switching to DOR

	Switch to DOR N = 388
Age, median (IQR)	56 (44, 61)
Female sex, n (%)[a]	83 (21)
Black race, n (%)	128 (33)
Hispanic ethnicity, n (%)	97 (25)
CD4 cell count, median cells/μL (IQR)	621 (443, 858)
Body weight (kg), median (IQR)	86 (75, 99)
BMI (kg/m^2), n (%)	
Underweight: <18.5	6 (1)
Normal: ≥18.5 to <25	81 (21)
Overweight: ≥25 to <30	150 (39)
Obese: ≥30	151 (39)

BMI, body mass index; DOR, doravirine; IQR, interquartile range; N, number.
[a] Among women: 70% were Black, 49% were ≥50 years old, 20% were 40-49 years old.

Figure 1. Changes in body weight after switching to a DOR-containing regimen, stratified by sex[a]



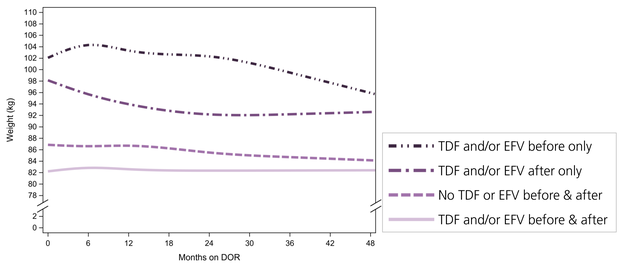
[a] Mean predicted weights estimated with univariate linear mixed model, restricted cubic splines on time (knots: 0, 6, 12, 24 months).

Table 2. Rates of change in body weight after switching to a DOR-containing regimen[a]

		N	Total # observations	# observations/person Median (IQR)	Rate of weight change kg/year (95% CI)
Overall		388	2539	5 (2, 9)	-0.80 (-1.32, -0.28)
By sex	Female	83	494	4 (2, 9)	-1.67 (-3.32, -0.02)
	Male	305	2045	5 (2, 9)	-0.60 (-1.12, -0.08)
By TDF and/or EFV use before & after switch	TDF and/or EFV before only	8	50	4 (2, 10)	-0.71 (-2.40, 0.98)
	TDF and/or EFV after only	86	498	4 (3, 8)	-2.22 (-4.03, -0.42)
	No TDF or EFV before & after	238	1539	5 (2, 9)	-0.72 (-1.31, -0.14)
	TDF and/or EFV before & after	56	452	7 (3, 10)	-0.05 (-1.22, 1.11)
By INSTI and TAF combination, if maintained	No INSTI, no TAF	18	107	5 (2, 8)	0.19 (-2.26, 2.65)
	No INSTI, TAF	28	161	4 (2, 8)	-0.40 (-2.01, 1.21)
	INSTI, TAF	100	668	5 (2, 8)	-0.45 (-1.31, 0.41)
	INSTI, no TAF	86	540	6 (2, 8)	-0.72 (-1.50, 0.05)

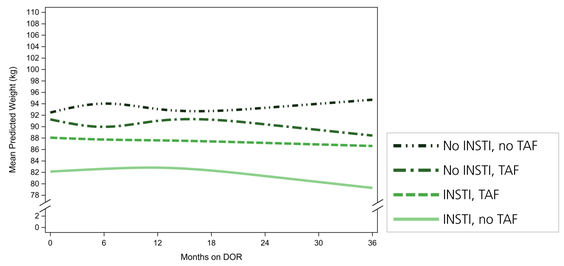
CI, confidence interval; DOR, doravirine; EFV, efavirenz; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; N, number; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.
[a] Rates of weight change estimated with univariate linear mixed model.

Figure 2. Weight changes by patterns of TDF and/or EFV use before and after switch to DOR[a]



[a] Mean predicted weights estimated with univariate linear mixed model, restricted cubic splines on time (knots: 0, 6, 12, 24 months).

Figure 3. Weight changes while maintaining the same INSTI/TAF combination before and after switch to DOR[a]



[a] Mean predicted weights estimated with univariate linear mixed model, restricted cubic splines on time (knots: 0, 6, 12, 24 months).

Discussion

- Of 388 virologically suppressed individuals switching to a DOR-containing regimen, 78% were overweight or obese at switch (**Table 1**).
- Overall, switching to DOR was associated with an average weight loss of 0.80 kg/year (**Fig 1**, **Table 2**).
  - Women lost weight at a rate of 1.67 kg/year; most were Black and of perimenopausal or menopausal age (**Tables 1-2**).
  - Men lost weight at a rate of 0.60 kg/year (**Table 2**).
- DOR was associated with weight loss in the absence of TDF and/or EFV before and after switch (**Fig 2**, **Table 2**).
- Among those who had the same INSTI-TAF combination before and after switching to DOR, there was a trend toward weight loss (not statistically significant) (**Fig 3**, **Table 2**).
- A modest weight loss on DOR is clinically meaningful given that most individuals included were overweight or obese at DOR start and that weight gain has often been associated with female sex.

Key Findings

- DOR was associated with a modest but statistically significant weight loss overall, especially in women.
- Patterns of use of antiretrovirals associated with weight gain (INSTI, TAF) or weight loss (TDF, EFV) did not fully explain the weight loss observed on DOR.

References

1. Kanters et al. Evidence synthesis evaluating body weight gain among people treating HIV with antiretroviral therapy - a systematic literature review and network meta-analysis. eClinicalMedicine. 2022.

Acknowledgements

This research would not be possible without the generosity of people living with HIV and their OPERA caregivers. Additionally, we are grateful for the following individuals: Robin Beckerman (SAS programming), Kelly Oh (QA), Bernie Stooks & Stephen Connellee (data architecture), Lisa Lutzi & Nicole Shaw (data management/quality), and Judy Johnson (clinical data categorization).

Support

This research was sponsored by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

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