Dolutegravir With Either Doravirine or Rilpivirine: Two-Drug Antiretroviral Therapy Outcomes

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BACKGROUND

- More people with HIV (PWH) are switching to two-drug, NRTI-sparing antiretroviral therapy (ART).
- In 2021, the FDA approved a fixed-dose combination of dolutegravir (DTG) and rilpivirine (RPV).
- When DTG+RPV isn't an option—due to proton pump inhibitor interactions or RPV resistance—DTG combined with doravirine (DOR) may offer an alternative free of NRTIs and protease inhibitors.
- Our study aimed to assess the efficacy of DTG+DOR while clinical trials continue.

OBJECTIVE: To compare virologic outcomes between PWH switching to either DTG+DOR or DTG+RPV.

METHODS

This analysis includes participants from the **DC Cohort**, an ongoing observational study of approximately 13,200 PWH receiving care in Washington, DC.

Inclusion Criteria:

1) Initiating or switching to DTG+DOR or DTG+RPV on or after July 2019 *and*

2) At least 1 year of observation post-regimen initiation.

Covariates:

Demographics, diagnoses, labs, antiretrovirals (ARV), ARV resistance mutations were extracted from electronic health records from 14 HIV clinics.

Independent Variable:

Regimen type (DTG+DOR **or** DTG+RPV)

Outcome Variable:

Time to first viral non-suppression (HIV RNA >200 copies/mL) post initiation.

Viral Load at Initiation:

Most recent viral load within 12 months prior to regimen initiation.

Statistical Analysis:

1) Differences for DTG+DOR and DTG+RPV were analyzed with **Chi-square tests** and **Wilcoxon Rank Sum tests.**

2) Among participants virally suppressed at regimen initiation, assessed viral loads ≥50 and ≥200 copies/mL at 12 and 24 months prior to regimen initiation.

3) Kaplan-Meier (K-M) Curves were used to identify risk factors for virologic non-suppression among participants virally suppressed at regimen initiation.

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A ***higher*** proportion of participants had durable viral suppression (<200 copies/mL) at 24 months on DTG+RPV (82.1%) compared to DTG+DOR (58.3%). Baseline differences such as longer treatment experience, prior viral non-suppression and resistance mutations, may account for these findings.

RESULTS

Table 1. Demographics and Clinical Characteristics for Participants on DOR+DTG or RPV+DTG

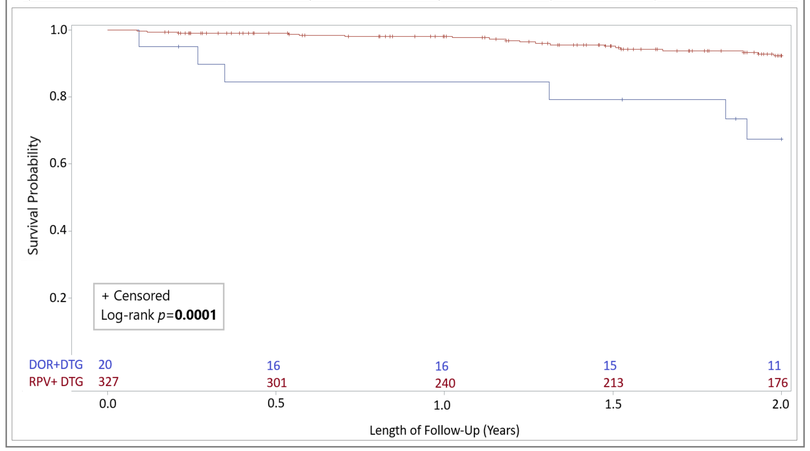
Characteristics	Total PWH N (%) 466	DOR+DTG N (%) 31	RPV+DTG N (%) 435	*p*-value
Age at Regimen Initiation, median (IQR)	58.3 (50.5-64.5)	62.0 (55.1-64.3)	58.0 (50.0-64.5)	0.0539
Race				0.5406
Black Non-Hispanic	367 (78.8)	27 (87.1)	340 (78.2)	
White Non-Hispanic	70 (15.0)	2 (6.5)	68 (15.6)	
Hispanic	10 (2.2)	1 (3.2)	9 (2.1)	
Other/Unk	19 (4.1)	1 (3.2)	18 (4.1)	
Sex at Birth				0.8341
Male	353 (75.8)	23 (74.2)	330 (75.9)	
Female	113 (24.3)	8 (25.8)	105 (24.1)	
Site Type				**0.0018**
Community	200 (42.9)	5 (16.1)	195 (44.8)	
Academic	266 (57.1)	26 (83.9)	240 (55.2)	
Time (Years) since HIV Diagnosis[1], median (IQR)	19.97 (12.1-25.7)	25.1 (16.3-30.7)	19.6 (11.3-25.3)	**0.0016**
Time (Years) since ARV Initiation[2], median (IQR)	12.32 (7.4-18.0)	18.4 (14.2-21.8)	11.5 (7.0-17.6)	**0.0001**
Insurance				**0.0054**
Private	152 (32.6)	2 (2.5)	150 (34.5)	
Public	288 (61.8)	27 (87.1)	261 (60.0)	
Unknown/Other	26 (5.6)	2 (2.5)	24 (5.5)	
Chronic Kidney Disease[3]	194 (41.6)	13 (41.9)	181 (41.6)	0.9716
CD4 (cells/mm³) at Initiation, Median (IQR)	598 (435-849)	634 (481-812)	595 (432-853)	0.7759
Virally Suppressed at Regimen Initiation	399 (85.6)	24 (77.4)	375 (86.2)	0.0900
Among Participants on Regimens who are Virally Suppressed at Regimen Initiation[4], N=399				
Time (Years) on Regimen[5], Median (IQR)	2.0 (1.0-2.0)	1.9 (1.2-2.0)	2.0 (1.0-2.0)	0.7306
Viral Load 12 months prior to Regimen Initiation				
Viral Load ≥50 copies/mL	62 (15.5)	7 (29.2)	55 (14.7)	0.0763
Viral Load ≥200 copies/mL	14 (3.5)	1 (4.2)	13 (3.5)	0.5866
Viral Load 24 months prior to Regimen Initiation				
Viral Load ≥50 copies/mL	107 (26.8)	7 (29.2)	100 (26.7)	0.8133
Viral Load ≥200 copies/mL	36 (9.0)	1 (4.2)	35 (9.3)	0.7113
Mutations Present (Pre- and Post-Regimen Initiation)				
NRTI	90 (22.56)	14 (58.3)	76 (20.3)	**<.0001**
NNRTI	73 (18.3)	12 (50.0)	61 (16.3)	**0.0003**
PI	75 (18.80)	12 (50.0)	63 (16. 8)	**0.0003**
INSTI	5 (1.3)	2 (8.3)	3 (0.8)	**0.0311**

1: There were 433 participants on RPV+DTG with an HIV diagnosis date. All participants on DOR+DTG had the date available.
2: N=306; There were 23 participants on DOR+DTG with ARV initiation date and 283 on RPV+DTG.
3: Chronic Kidney Disease Stages III, IV, V, including dialysis and kidney replacement therapy.
4: Any HIV RNA result within 12 months or 24 months prior to regimen initiation above the threshold.
5: Regimens include DTG+DOR or DTG+RPV where the maximum observation time was 24 months.

RESULTS

- PWH on DTG+DOR were more likely to have public insurance and receive care at an academic site than the PWH on DTG+RPV.
- In the 12 months before regimen initiation, 29.2% of DTG+DOR participants had viral loads ≥50 copies/mL versus 14.7% for DTG+RPV.
- Time living with HIV and on ARV was longer for those on DTG+DOR.
- Resistance mutations were more common among those on DTG+DOR.
- Viral suppression at regimen initiation (399/466) was 77.4% (24/31) for DTG+DOR compared to 86.2% (375/435) for DTG+RPV.

Figure 1. Kaplan-Meier Curve for Time to Viral Non-Suppression (HIV RNA ≥ 200 copies/mL) Stratified by Two-Drug ARV Regimen, ***N=399***



- The log-rank test indicated ***significant*** difference between K-M curves for each regimen (p= 0.0001) with 82.1% virally suppressed on DTG+RPV at 24 months compared to 58.3% on DTG+DOR .

CONCLUSIONS

- Durable viral suppression was lower with DTG+DOR, possibly due to baseline differences.
- DTG+DOR might be an effective two-drug regimen, but caution is advised with baseline resistance or prior viral non-suppression.
- Future research will use adjusted or propensity score analyses to account for potential baseline differences.
- Prospective switching studies are needed to evaluate the long-term outcomes of DOR+DTG with other two-drug regimens.

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