2-Drug Regimen Comparable to 3-Drug Regimens up to 18 Months in a Real-World Setting

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Background

- Three antiretrovirals from two classes have long been the standard of care for people living with HIV (PLWH)[1-4]
- Newer, more powerful antiretrovirals have introduced the potential for effective therapy with fewer agents[5,6]
- Dolutegravir/rilpivirine (DTG/RPV) was the first single-tablet, once-daily regimen containing only two antiretrovirals to be approved (late 2017)[7]

OBJECTIVE

To compare the effectiveness and durability of DTG/RPV to standard three-drug regimens (3-DR) in a real-world setting

Methods

Study population

- Data source: OPERA database of electronic health records from 105,643 PLWH (148 cities in U.S. and Puerto Rico) as of 12 July 2019
- Inclusion Criteria:
  - » HIV- 1 positive, HIV-2 negative, ≥13 years of age
  - » Initiated a 2-DR (DTG/RPV) or 3-DR (DTG, EVG, RAL, DRV, RPV, or ATV + 2 NRTIs, boosted or unboosted) between 1 Jan 2018 and 31 Dec 2018
  - » Last viral load <50 copies/mL on or before initiation of regimen of interest
  - » No exposure to DTG/RPV prior to initiation
- Baseline: Date of initiation of 2-DR or 3-DR of interest
- Study outcomes:
  - » Virologic failure: 2 VL ≥ 200 copies/mL or 1 VL ≥ 200 copies/mL + regimen discontinuation
  - » Sustained suppression: Last VL <50 copies/mL and <200 copies/mL
  - » Treatment discontinuation: Modification or discontinuation of regimen of interest
- Follow-up until:
  - » Regimen discontinuation
  - » Death
  - » Study end (30 June 2019)

Analyses

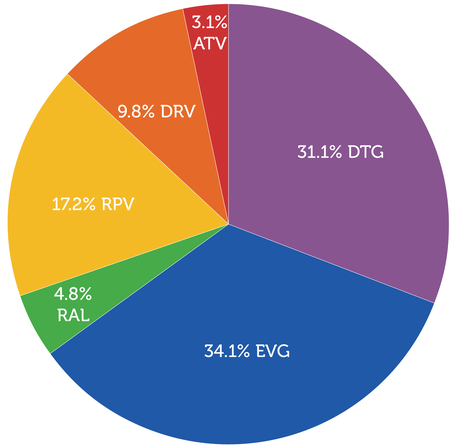
- Description of patient characteristics and outcomes
  - » Categorical variables: Pearson's chi-square or Fisher exact tests
  - » Continuous variables: Wilcoxon rank-sum
- Time to discontinuation and virologic failure
  - » Kaplan-Meier methods
  - » Multivariable Cox Proportional Hazards models

Results

Table 1. Baseline demographic and clinical characteristics

Characteristic n (%)	DTG/RPV (n=545)	3-DR (n=5,524)	p-value
Age ≥50 years	298 (54.7%)	2,258 (40.9%)	<.0001
Female sex	97 (17.8%)	1,078 (19.5%)	0.5199
Black race	177 (32.5%)	2,445 (44.3%)	<.0001
Hispanic ethnicity	163 (29.9%)	1,139 (20.6%)	<.0001
Care in Southern US	350 (64.2%)	3,146 (57.0%)	<.0001
Hx of AIDS	146 (26.8%)	1,565 (28.3%)	0.4453
CD4 Count >500 cells/ µL	424 (77.8%)	3,959 (71.7%)	0.0178
Hx of Syphilis	164 (30.1%)	1,895 (34.3%)	0.0475
Any Comorbidity	475 (87.2%)	4,416 (79.9%)	<.0001

Figure 1. Distribution of core agents in the 3-DR group*



*DTG = Dolutegravir, EVG = Elvitegravir, RAL = raltegravir, RIL = rilpivirine, DRV = darunavir, ATV = Atazanavir

Table 2. Durability and virologic suppression with 2-DR versus 3-DR

Outcome (n, % or median, IQR)	DTG/RPV (n=545)	3-DR (n=5,524)	p-value
Durability			
Months on regimen	11.0 (8.2–14.2)	10.6 (6.8-14.6)	0.1432
Discontinuations	82 (15.0%)	1,544 (28.0%)	<.0001
Suppression among those tested			
Last VL < 50 copies/mL	457 (94.0%)	3,984 (89.0%)	0.0006
Last VL < 200 copies/mL	475 (97.7%)	4,275 (95.5%)	0.0221

Figure 2. Unadjusted cumulative probability of discontinuation of 2-DR versus 3-DR

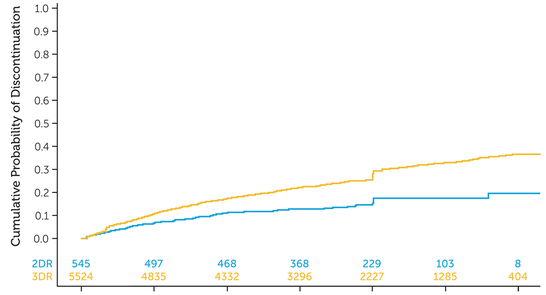


Figure 3. Unadjusted cumulative probability of virologic failure of 2-DR versus 3-DR

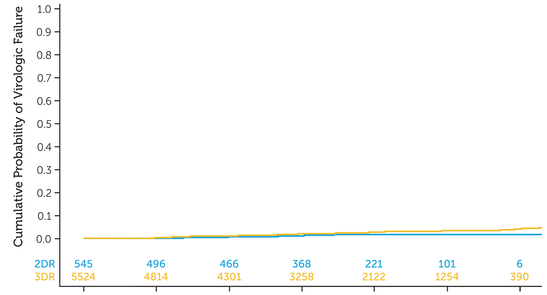


Table 3. Virologic Failure with 2-DR versus 3-DR

Virologic Failure among those tested	DTG/RPV (n=545)	3-DR (n=5,524)	p-value
Virologic Failures, n (%)	7 (1.4%)	124 (2.8%)	0.0823
Incidence Rate (95% CI)*	1.45 (0.69, 3.03)	2.63 (2.21, 3.14)	0.1422
Unadjusted HR (95% CI)†	1.0	1.38 (0.43, 4.43)	0.1279
Adjusted HR (95% CI)‡	1.0	1.32 (0.61, 2.90)	0.4813

*per 100 person-years
†HR=Hazard Ratio
‡HR adjusted for age, sex, race, ethnicity, region, CD4 cell count, history of comorbidities

Discussion

- DTG/RPV users differed from 3-DR users notably (Table 1)
  - » DTG/RPV users were older, more likely to be Hispanic, to live in the southern US, and have comorbidities
  - » 3-DR users were younger, more likely to be African American, and have a history of syphilis (an indicator of a complex lifestyle)
- DTG/RPV users experienced fewer discontinuations and were more likely to be suppressed at study end compared to 3-DR users (Table 2, Figure 2)
- Virologic failure was uncommon and did not differ between DTG/RPV and 3-DR users (Table 3, Figure 3)
- Strengths: Large, diverse population of PLWH in the US
- Limitations: No reasons for discontinuation or resistance data for those who failed

KEY FINDINGS

Among ART-experienced, virologically suppressed PLWH initiating DTG/RPV or standard 3-DR, there was no observed difference in their risk of virological failure in a real-world setting over the first 18 months of approval

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