Poster: 1265

Effectiveness and Durability of Dolutegravir (DTG) Based Regimens in Older People Living With HIV (PLWH) From the Veterans Aging Cohort Study (VACS)

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Introduction

- HIV management among older people living with HIV (PLWH) may be complicated by the presence of multiple comorbidities and polypharmacy. [1,2]
- There is currently limited data on treatment patterns and clinical outcomes in older PLWH, particularly for newer drug classes like integrase strand transfer inhibitors (INSTIs).
- The Veterans Aging Cohort (VACS) is a large-scale research study that includes data from > 60,000 veterans with HIV, the majority being ≥ 50 years of age.
- Utilizing data from the VACS, this study evaluated effectiveness and durability of modern 3-drug antiretroviral regimens among older PLWH.

Methods

Study Population

- Retrospective observational cohort study utilizing electronic health record and pharmacy data from the VACS
- Inclusion criteria:
  - A diagnosis of HIV-1
  - Prescribed a regimen containing the core agents dolutegravir (DTG), bictegravir (BIC), elvitegravir (EVG), raltegravir (RAL), or darunavir (DRV) plus 2 nucleoside reverse transcriptase inhibitors (NRTIs) for the first time between 1/1/2014 and 3/31/2020
  - Age ≥ 50 when initiating the regimen

Follow-up

- Included PLWH were followed from regimen initiation (baseline) until regimen discontinuation, death, loss to follow-up, or end of study (9/30/2020).

Outcome Definitions

- Suppression: viral load (VL) < 50 copies/mL
- Low-viremia: 50 copies/mL ≤ VL < 200 copies/mL
- Virologic failure: 2 consecutive VLs ≥ 200 copies/mL, or 1 VL ≥ 200 copies/mL followed by regimen discontinuation within 4 months
- Regimen discontinuation: change in regimen core agent
- Change in CD4 cell count: change in CD4 cells/µL between baseline and 6- and 12-months post-baseline

Statistical Methods

- Outcomes were stratified by antiretroviral therapy (ART) experience (ART-naive and ART-experienced).
- Pairwise comparison was made between DTG-based regimen and each of the other 3-drug regimens with DTG as the referent.
- Outcomes were compared using linear regression or logistic regression (all other outcomes).
- Inverse probability of treatment weighting was used to adjust for confounding by treatment assignment. Variables included: age, sex, race/ethnicity, region, smoking status, alcohol use, drug use, homelessness status, time on ART, baseline CD4 cell count, baseline viral load, and baseline VACS index.

Results

Table 1. Baseline characteristics of ART-naive PLWH

	DTG (N=912)	BIC (N=432)	EVG (N=751)	RAL (N=159)	DRV (N=235)
Sex: Male, n (%)	864 (95)	420 (97)	720 (96)	154 (97)	228 (97)
Age (≥ 65), n (%)	204 (22)	120 (26)	157 (21)	34 (21)	62 (26)
Race/Ethnicity, n (%)					
Hispanic	44 (5)	36 (8)	46 (6)	20 (13)	22 (9)
Black	472 (52)	212 (49)	370 (49)	69 (43)	123 (52)
White	331 (36)	158 (37)	293 (39)	64 (40)	76 (32)
Other	65 (7)	26 (6)	42 (6)	6 (4)	14 (6)
Smoking status, n (%)					
Current	446 (49)	182 (42)	338 (45)	88 (55)	113 (48)
Past	283 (31)	157 (36)	243 (32)	34 (21)	68 (29)
Never/Unknown	83 (20)	93 (22)	170 (23)	37 (23)	54 (23)
Unhealthy alcohol use or alcohol-related diagnosis (recent 12m), n (%)	196 (22)	95 (22)	182 (24)	35 (22)	46 (20)
Drug abuse and dependence[1] (recent 12m), n (%)	128 (14)	55 (13)	98 (13)	32 (20)	37 (16)
Homeless (recent 12m), n (%)	103 (11)	48 (11)	90 (12)	20 (13)	37 (16)
Hepatitis C coinfection, n (%)	47 (5.2)	28 (6.5)	36 (4.8)	10 (6.3)	8 (3.4)
Charlson comorbidity index, mean (sd)	7.8 (2.1)	7.9 (2.0)	7.3 (1.8)	8.0 (2.3)	7.5 (1.9)
CD4 (cells/µL), mean (sd)	439 (288)	431 (300)	441 (279)	419 (298)	324 (268)
Viral load (log copies/mL), mean (sd)	4.5 (0.8)	4.4 (0.9)	4.5 (0.8)	4.4 (0.9)	4.4 (0.9)
Virologically suppressed[2], n (%)	209 (28)	116 (32)	172 (28)	38 (33)	59 (33)
Low viremia[2], n (%)	25 (3.4)	12 (3.3)	31 (5.1)	6 (5.2)	11 (6.2)
VACS index 2.0, mean (sd)	61 (20)	60 (19)	58 (17)	62 (20)	66 (22)
Number of non-ARV co-medications, mean (sd)	9 (7)	8 (7)	8 (6)	8 (6)	7 (6)
Tenofovir- or abacavir-containing regimen, n (%)	908 (100)	432 (100)	751 (100)	155 (98)	228 (97)

Table 2. Baseline characteristics of ART-experienced PLWH

	DTG (N=5097)	BIC (N=1765)	EVG (N=3580)	RAL (N=1486)	DRV (N=1879)
Sex: Male, n (%)	4952 (97)	1713 (97)	3482 (97)	1440 (97)	1834 (98)
Age (≥ 65), n (%)	1747 (34)	670 (38)	993 (28)	475 (32)	448 (24)
Race/Ethnicity, n (%)					
Hispanic	297 (6)	154 (9)	278 (8)	162 (11)	123 (7)
Black	2627 (52)	822 (47)	1753 (49)	650 (44)	1126 (60)
White	1972 (39)	719 (41)	1390 (39)	626 (42)	553 (29)
Other	201 (4)	70 (4)	161 (4)	48 (3)	78 (4)
Smoking status, n (%)					
Current	2575 (51)	819 (46)	1719 (48)	768 (52)	1084 (58)
Past	1436 (28)	558 (32)	1061 (30)	381 (26)	476 (25)
Never/Unknown	1086 (21)	388 (22)	800 (22)	337 (23)	319 (17)
Unhealthy alcohol use or alcohol-related diagnosis (recent 12m), n (%)	985 (19)	310 (18)	626 (18)	266 (18)	409 (22)
Drug abuse and dependence[1] (recent 12m), n (%)	847 (17)	228 (13)	490 (14)	249 (17)	418 (22)
Homeless (recent 12m), n (%)	459 (9)	133 (8)	320 (9)	126 (9)	253 (14)
Hepatitis C coinfection, n (%)	946 (19)	209 (12)	435 (12)	365 (25)	412 (22)
Charlson comorbidity index, mean (sd)	8.9 (2.7)	8.3 (2.4)	8.2 (2.3)	9.3 (3.0)	8.7 (2.5)
CD4 (cells/µL), mean (sd)	567 (270)	610 (265)	568 (270)	516 (270)	467 (274)
Viral load (log copies/mL), mean (sd)	3.5 (0.7)	3.5 (0.7)	3.5 (0.8)	3.5 (0.7)	3.8 (0.9)
Virologically suppressed[2], n (%)	3760 (79)	1306 (82)	2493 (76)	1026 (79)	1028 (62)
Low viremia[2], n (%)	345 (7.3)	95 (6.0)	225 (6.9)	88 (6.7)	173 (10)
VACS index 2.0, mean (sd)	51 (18)	51 (16)	47 (16)	54 (18)	56 (19)
Number of non-ARV co-medications, mean (sd)	11 (7)	10 (7)	9 (6)	12 (7)	11 (7)
Time on ARV (years), mean (sd)	12.2 (6.7)	13.8 (6.9)	11.9 (6.6)	12.0 (6.9)	12.1 (6.8)
Tenofovir- or abacavir-containing regimen, n (%)	5054 (99)	1765 (100)	3580 (100)	1394 (94)	1798 (96)

[1] Opioids, amphetamines, cannabis, cocaine, hallucinogens, sedatives, hypnotics, anxiolytics, tranquilizers, and barbiturates.
[2] The proportions were calculated based on the number of those who had a viral load measurement.

Figure 1. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of treatment outcomes for those receiving BIC-, EVG-, RAL-, and DRV-based 3-drug regimens compared to those receiving DTG-based 3-drug regimen

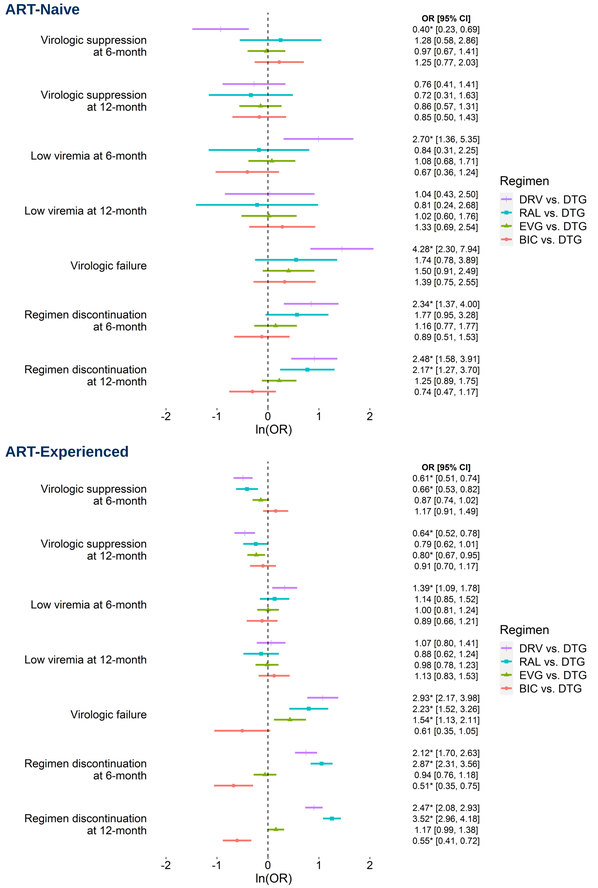


Figure 2. Mean differences (95% CIs) of change in CD4 cell count from baseline to the end of 6 months

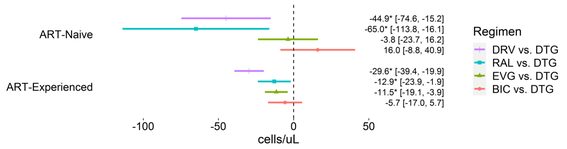
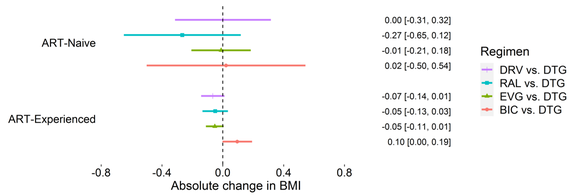


Figure 3. Mean difference of absolute change in BMI at 6 months



Results Summaries

Virological measures and duration of regimens (Figure 1)

- Those on DTG were more likely suppressed at 6 months compared to those on DRV among ART-naive PLWH, and more likely suppressed at 6 and 12 months compared to DRV and RAL among ART-experienced PLWH.
- DTG-based regimens demonstrated reduced odds of virologic failure compared to DRV among ART-naive and compared to DRV, RAL, and EVG among ART-experienced PLWH.
- Regardless of ART experience, discontinuation was higher for RAL and DRV compared to DTG. Discontinuation was lower for BIC compared to DTG at 6 and 12 months among ART-experienced PLWH.
  - Discontinuations of DTG-based regimen at 12 months included 52% switching from multi-tablet regimen to single-tablet regimen, and 47% switching to remove abacavir from the regimen.

Immunological measures (Figure 2)

- For both naive and experienced PLWH, those on DTG had greater increases in CD4 cell counts at 6 and 12 months compared to those on DRV or RAL.

Safety outcomes (Figure 3)

- Change in BMI was comparable between regimens 6-months post-baseline.
- Changes in blood pressure and lipids over 12 months of baseline regimen exposure were comparable, although missing data were frequent and confidence intervals were wide (data not shown).

Conclusions

- For both ART-naive and ART-experienced PLWH > 50 years old, treatment responses during the first 12 months of follow-up were similar for those taking DTG-, BIC-, and EVG-based regimens.
- DTG-based regimens demonstrated greater effectiveness and durability compared to DRV- or RAL-based regimens.

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Acknowledgments: This research was sponsored by ViiV Healthcare. This study was supported by the Veterans Aging Cohort Study, which is a CHAART Cooperative Agreement funded by National Institutes of Health NIAAA (P01 AA029545, U24-AA020794, U01-AA020790, U24-AA022001, U01-AA026224, U10 AA013566-completed) and in kind by the US Department of Veterans Affairs. The VACS study was approved by the institutional review boards of Yale University (ref Yale: 0309025943) and VA Connecticut Healthcare System (ref VA: AJ0001). It has been granted a waiver of informed consent and is compliant with the Health Insurance Portability and Accountability Act.

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