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DOLUTEGRAVIR IS ASSOCIATED WITH MORE DEPRESSIVE SYMPTOMS IN OLDER PEOPLE WITH HIV

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Objective

Determine the relationships between integrase strand transfer inhibitors (InSTIs), aging, antidepressant use, and depressive symptoms in people with HIV (PWH).

Background

- InSTIs such as dolutegravir (DTG) are first-line therapy in the U.S. and other countries.
- DTG has been linked to neuropsychiatric adverse events (e.g., depression) in PWH. However, standardized assessments of depression among PWH taking DTG was not well characterized.
- The present study has investigated the concomitant influence of age and antidepressant use on depression among DTG users in CHARTER cohort.

Results

Table 1. Demographic, Disease, and Treatment Characteristics of the Cohort Stratified by Use of DTG, Other InSTIs, or Other ART.

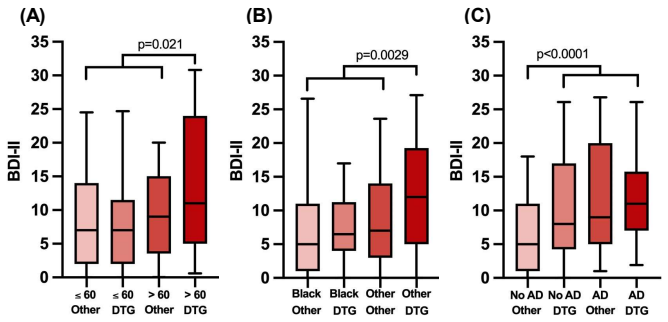
Characteristic	Total Cohort	DTG Users	Other InSTI Users	Non-InSTI Users	P value
Group Size	280	95	94	91	
Age (years)	56.2 (8.0)	56.8 (7.7)	55.9 (7.9)	55.8 (8.5)	0.631
Age ≥ 60 years	81 (28.9%)	31 (32.6%)	24 (25.5%)	26 (28.6%)	0.558
Gender (Female)	52 (18.6%)	23 (24.2%)	16 (17.0%)	13 (14.3%)	0.202
Race (Black)	109 (38.9%)	37 (38.9%)	40 (42.6%)	32 (35.2%)	0.589
Ethnicity (Hispanic)	32 (11.4%)	6 (6.3%)	10 (10.6%)	16 (17.6%)	0.052
Body Mass Index	26.4 (8.7)	27.8 (8.7)	26.5 (8.2)	24.7 (9.0)	0.047
HCV Seropositive	94 (33.6%)	36 (37.9%)	27 (28.7%)	31 (34.1%)	0.405
Diabetes Mellitus	58 (20.7%)	26 (27.4%)	17 (18.1%)	15 (16.5%)	0.146
Hypertension	151 (53.9%)	55 (57.9%)	58 (61.7%)	38 (41.8%)	0.016
Dyslipidemia	117 (41.8%)	44 (46.3%)	44 (46.8%)	29 (31.9%)	0.062
Chronic Pulmonary Disease	61 (21.8%)	21 (22.1%)	24 (25.5%)	16 (17.6%)	0.418
Antidepressant Use	93 (33.2%)	27 (28.4%)	34 (36.2%)	32 (35.2%)	0.465
Lifetime Major Depressive Disorder	179 (63.9%)	64 (67.4%)	62 (66.0%)	53 (58.2%)	0.384
Current Major Depressive Disorder	20 (7.7%)	9 (9.8%)	7 (8.0%)	4 (4.9%)	0.469
Duration of HIV infection (years)	22.3 (6.6)	22.8 (6.4)	22.5 (6.6)	21.8 (6.8)	0.598
AIDS Diagnosis	203 (72.5%)	77 (81.0%)	65 (69.1%)	61 (67.0%)	0.061
Tenofovir Alafenamide Use	128 (45.7%)	25 (26.3%)	74 (78.7%)	29 (31.9%)	<0.001
Abacavir Use	69 (24.6%)	50 (52.6%)	4 (4.3%)	15 (16.5%)	<0.001
Total duration of all ART (years)	15.6 (6.0)	15.3 (5.8)	15.7 (6.4)	15.8 (5.8)	0.843
Duration of current regimen (mths)	38.0 (44.8)	25.9 (26.2)	22.2 (25.2)	66.5 (59.7)	<0.001
Plasma HIV RNA (≤ 200 cp/mL)	280 (100%)	95 (100%)	94 (100%)	91 (100%)	*
Nadir CD4+ T-Cell Count	156.1 (152.6)	134.4 (142.1)	164.6 (165.0)	170.0 (148.8)	0.227
CD4+ T-Cell Count	622.8 (315.8)	581.9 (296.9)	639.0 (348.0)	649.4 (299.1)	0.291

Conclusions

- **Dolutegravir may increase depressive symptoms in PWH who are at least 60 years old, who are not using an antidepressant, or whose race is other than Black.**
- **Conversely, dolutegravir was not associated with more depressive symptoms in PWH who were younger than 60 years, who were taking an antidepressant, or whose race was Black.**
- **This is the first study to use a standardized depression assessment and to identify an interaction with antidepressant drugs.**

Results

Figure 1. DTG was associated with higher BDI-II values (A) in people who were at least 60 years old, (B) people whose race was not Black, and (C) people who did not use an antidepressant drug (AD)



Results

Table 2. Regression analysis of dependent variable used in this study

Independent Variable	Standard β	P Value	Standard β	P Value
Antidepressant Use	0.164	**0.002**	0.124	**0.049**
Race	0.211	**<0.001**	0.216	**<0.001**
Gender	0.122	**0.042**	0.160	**0.008**
Dolutegravir Use	0.130	**0.029**	0.189	**0.009**
Age ≤ or > 60 years	0.114	**0.056**	0.111	**0.063**
Dolutegravir x Age ≤ or > 60 years	-	-	0.123	**0.059**
Dolutegravir x Race	-	-	0.116	**0.060**
Dolutegravir x Antidepressant Use	-	-	0.128	**0.083**
Abacavir Use	0.077	0.199		
Duration of current regimen	-0.065	0.290		
AIDS Diagnosis	-0.052	0.383		
Body Mass Index	0.037	0.536		
Dyslipidemia	0.032	0.571		
Tenofovir Alafenamide Use	0.032	0.597		
Ethnicity (Hispanic)	0.017	0.774		
Other InSTI Use	0.012	0.863		
Age (years)	0.007	0.905		

- As summarized in Table 1, participants had a mean age of 56.2 years (28.9% ≥ 60), 18.6% were women, 38.9% identified as Black race, and 72.5% had an AIDS diagnosis. The mean CD4+ T-cell count was 622.8/μL.
- The mean duration of the current ART regimen was 38.0 months and more than two-thirds of participants were using an InSTI.
- Overall, InSTI use was not associated with BDI-II values but DTG use trended toward association with worse BDI-II scores (p=0.064), particularly in the Apathy subscale (p=0.019).
- As summarized in Table 2, multivariable analysis identified that DTG use (p=0.009), non-Black race (p<0.001), female gender (p=0.008), and age > 60 (p=0.063) were associated with worse BDI-II scores.
- Interactions with DTG use selected by Akaike Information Criterion included ones with age category, antidepressant use, and race. These are shown graphically in Figure 1.

Methods

- 280 participants were comprehensively assessed in the CHARTER Aging project. All were were taking ART and had plasma HIV RNA ≤ 200 copies/mL.
- Beck Depression Inventory (BDI)-II and four subscales were compared to demographic characteristics, use of InSTIs and antidepressants, and clinical biomarkers in a cross-sectional design
- Data were analyzed using linear regression, including multivariable linear regression with backward selection by Akaike Information Criterion.

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