DTG prescribing patterns in PLWH ≥ 65 years: the impact of 2DR and weight gain

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Background

Body composition changes, including obesity and accentuated aging has also been widely described in people living with HIV (PLWH). The level of complexity of this interaction in this population is further increased due to a possible association of modern antiretroviral therapy (ART) initiation or switching and weight gain (WG).

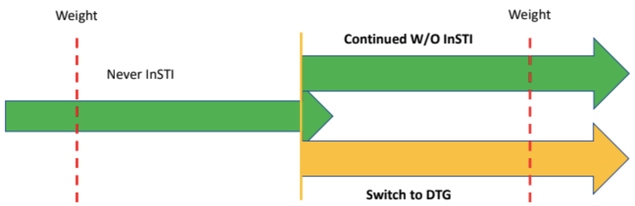
No randomised clinical studies assessed antiretroviral (ART) prescription specifically in geriatric HIV patients and its impact in weight gain.

Data can be obtained from observational studies or geriatric HIV cohorts. One of the largest geriatric HIV cohort is Geriatric Patients Living with HIV/AIDS (GEPPO) cohort. This is a prospective observational multicentre cohort started in 2015, including consecutive HIV-positive geriatric patients aged>65 years, and HIV negative controls, in care at 10 HIV clinics in Northern Central and Southern Italy.

The aim of this study was to explore weight gain in people living with HIV (PLWH) ≥65 years who switch to a DTG based regimen (DTG-s) vs remaining INSTI-naive (INSTI-n) on stable ART.

Methods

People were prospectively recruited in the GEPPO cohort. At cohort recruitment, participants were INSTI-naives (INSTI-n). During follow up they were divided in two groups: INSTI-n vs dolutegravir-switchers (DTG-s) with no further change in ART. Body weight was assessed at 1st study visit and at last evaluation. In the DTG-s group, the 1st visit was prior to switch. Weight was assessed with stadiometer during patient visit, asking patient to be in underwear without shoes.



Significant weight gain was defined **as an increase of ≥5% from 1st visit weight** over a follow-up.

ARV regimen was collected at patient visit with indication of the date of start of any drug. Regimens were classified as 2DR if included either 1INSTI or 1 PI and 1NNRTI or 3TC. Regimens were classified as 2DR if included 1INSTI+2NRTI, or 1PIc/r+2NRTI or 1NNRTI+2NRTI. Current exposure to TDF, TAF or ABC was specified.

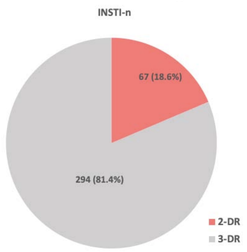
Figure 1 depicts study design. Weight gain assessment was preformed at baseline and at follow-up visit.

Statistical analyses

Results were expressed as mean and standard deviation (± SD), or median and interquartile range (IQR) for continuous variables based on the normality of distribution, and as frequencies and percentages for categorical variables. Kaplan-Meier plots and log-rank tests were used to illustrate time to reach a significant weight gain according to the "a priori" outcome measure definition. In order to explore the impact of ARTV regimens 3 different models were built comparing INSTI-n vs DTG-s, TAF vs TDF or 2DR vs 3DR.

Results and discussion

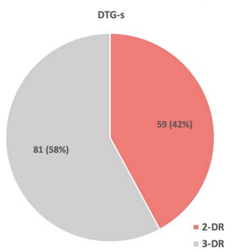
Out of 568 PLWH (16.9% females), 141 were in the DTG and 427 in the INSTI-n group. After an average follow up of 2.6 (±0.8) years, we did not observe significant difference in CD4 (673 vs 663 cell/microL, p=0.8) or virologic suppression (96.3% vs. 96.2%, p=0.99).



2-DR	
DRV + ABC	5 (7.5%)
ATV + 3TC	9 (13.4%)
DRV + ETR	7 (10.4%)
DRV + 3TC	8 (11.9%)
DRV/c + 3TC	11 (16.4%)
Others	27 (40.3%)

3-DR	
ATV + ABC/3TC	16 (5.4%)
EFV + ABC/3TC	12 (4.1%)
NEV + ABC/3TC	29 (9.9%)
EFV/FTC/TDF	15 (5.1%)
RPV/FTC/TAF	91 (31%)
Others	131 (44.6%)

Figure 2 shows proportion of 2DR and 3DR regimens in INSTI-n PLWH with most used ones in both groups.



2-DR	
DTG + ATV	5 (8.5%)
DTG + DRV/c	6 (10.2%)
DTG + 3TC	34 (57.6%)
DTG + RPV	10 (16.9%)
Others	4 (6.8%)

3-DR	
DTG/ABC/3TC	43 (53.1%)
DTG + DRV/c + 3TC	2 (2.4%)
DTG + FTC/TAF	34 (42%)
DTG + FTC/TDF	1 (1.2%)
Others	1 (1.2%)

Figure 3 shows proportion of 2DR and 3DR regimens in DTG-s PLWH with most used ones in both groups.

***Table 1** shows demographic, anthropometric and HIV characteristics both at baseline and follow-up. The prevalence of co-morbidities is provided only for baseline visit.*

	INSTI-n (N=427)	DTG-s (N=141)	p value
Age, years, mean (SD)	73.3 (4.7)	73.5 (4.7)	0.65
Males (%)	360 (84.3%)	112 (79.4%)	0.19
HIV exposure, years, mean (SD)	18.9 (7.1)	18.8 (7.4)	0.78
Body weight at first visit, kg, mean (SD)	74.5 (13.9)	71.8 (13.4)	0.09
HIV undetectability at first visit, %	95%	92.9%	0.99
Current CD4 at first visit, cell/microL, mean (SD)	650.7 (235.4)	652.9 (277)	0.69
ARV regimen at first visit			
PI, %	191 (44.7%)	77 (54.6%)	0.04
NNRTI, %	215 (50.4%)	49 (34.8%)	< 0.001
Current TDF exposure, %	148 (34.7%)	44 (31.2%)	0.47
Current ABC exposure, %	129 (30.2%)	53 (37.6%)	0.12
Comorbidities, first visit			
Chronic kidney disease, %	90 (27.8%)	56 (44.1%)	0.001
Osteoporosis, %	74 (23.8%)	44 (35.5%)	0.02
Cardiovascular disease, %	36 (11.4%)	13 (10.3%)	0.87
Dyslipidemia, %	162 (52.6%)	73 (61.3%)	0.11
Lipodystrophy, %	103 (35.2%)	42 (37.5%)	0.73
Type 2 diabetes mellitus, %	81 (25.3%)	25 (20.2%)	0.25
Hypertension, %	208 (63.6%)	93 (73.8%)	0.05
Cancer, %	46 (14.4%)	35 (27.1%)	0.004
Cirrhosis, %	26 (8.0%)	5 (3.9%)	0.15
Chronic obstructive pulmonary disease, %	17 (5.4%)	6 (4.8%)	0.85
Multimorbidity (at least 3 comorbidities), %	165 (38.6%)	79 (56.0%)	< 0.001
Polypharmacy (>5 medications), %	81 (19.0%)	30 (21.3%)	0.612
Body weight at last vist			
Body weight, kg, mean (SD)	74.1 (14.9)	71.0 (13.3)	0.06
Delta weight, kg, mean (SD)	0.02 (7.5)	-0.04 (5.2)	0.97
Weight gain >5% between first and last visit, %	19 (9.3%)	13 (15.1%)	0.175
HIV undetectability at last visit, %	92.6%	96.0%	0.44
Current CD4, at last visit, cell/microL, mean (SD)	663.9 (288.8)	673.4 (314.0)	0.82
ARV regimen at last visit			
PI, %	191 (44.7%)	77 (54.6%)	0.05
NNRTI, %	216 (50.6%)	13 (9.2%)	< 0.001
Current TAF exposure, %	141 (33.0%)	36 (25.5%)	0.12
Current TDF exposure, %	38 (8.9%)	0 (0.0%)	< 0.001
Current ABC exposure, %	103 (24.1%)	43 (30.5%)	0.13

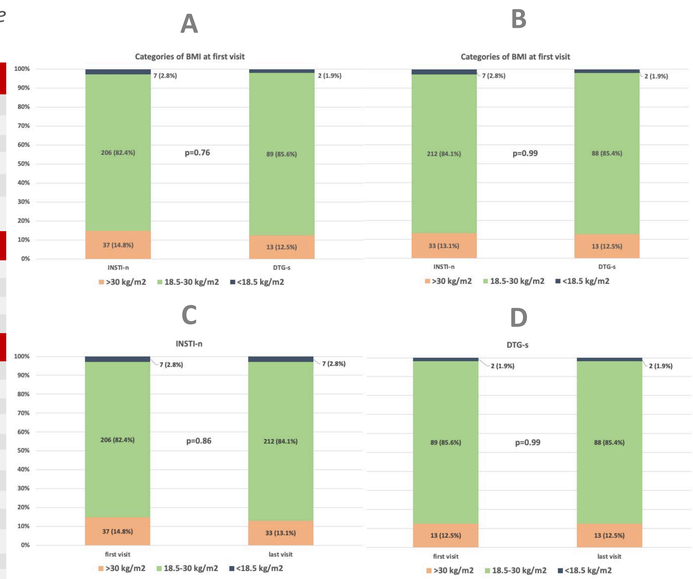


***Figure 4** depicts categories of BMI at the first and the last visit in both study arms. Panel A shows both study arms at first visit. Panel B shows both study arms at last visit. Panel C shows INSTI-n group at both baseline and follow-up. Panel D shows DTG-s at both baseline and follow-up. No statistical significance was observed.*

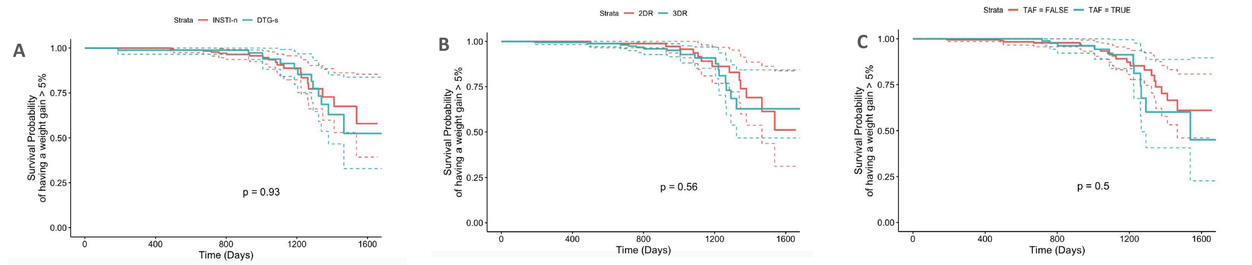


Figure 5 shows Kaplan-Meier plots to illustrate time to reach a significant weight gain in 3 different models comparing INSTI-n vs DTG-s (panel A), TAF vs TDF (panel B) or 2DR vs 3DR (panel C). No statistical significance was observed.

Conclusion

- At baseline we observed that PLWH who switched to DTG had higher burden of MM at baseline, possibly due to the selection of more vulnerable population for DTG regimens.
- DTG offers to vulnerable PLWH > 65 years a unique opportunity to avoid TDF or ABC toxicities regimens, which is explained by higher proportion of 2DR regimens observed in this study arm.
- 2-DR may be considered as a deprescribing recommendation in elderly.
- GEPPO cohort did not reveal a significant WG associated with switch to DTG in PLWH over 65 years of age, indicating that this phenomenon is not present in geriatric PLWH.
- This finding was confirmed comparing 3DR vs 2DR and TAF exposed vs unexposed geriatric PLWH.

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