Abstract PE2/55

Dolutegravir-based regimens are associated with weight gain over two years following ART-initiation in ART-naïve people living with HIV (PLWH)

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BACKGROUND

- Weight gain is common among people living with HIV (PLWH) after antiretroviral therapy (ART) initiation
- PLWH who initiate integrase inhibitor-based regimens may gain more weight than those who initiate other regimens
- Previous studies have examined classes not individual agents, been small, combined PLWH who were ART-experienced and naïve, and did not address potential confounders, such as anti-psychotic medications, which impact weight
- Previous studies have not included data assessing differences in regimen backbones, such as TDF vs. TAF
- This study evaluated weight change among PLWH initiating their first ART regimen

METHODS

- Study conducted in the Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) and included previously ART-naïve PLWH in clinical care at eight sites across the US from 2012-2018
  - CNICS data repository captures comprehensive clinical information from outpatient and inpatient encounters including medication data, diagnoses, and historical clinical information collected at initial clinic visit
- The 10 most common regimens with a minimum of 90 PLWH initiators were included in analyses

Regimen	Core Class	Drug 1	Drug 2	Drug 3	Drug 4
EFV	NNRTI	Efavirenz	Emtricitabine/Lamivudine	TDF	
RPV	NNRTI	Rilpivirine	Emtricitabine/Lamivudine	TDF	
ATV	PI	Atazanavir	Emtricitabine/Lamivudine	TDF	Ritonavir
DRV	PI	Darunavir	Emtricitabine/Lamivudine	TDF	Ritonavir
RAL	INSTI	Raltegravir	Emtricitabine/Lamivudine	TDF	
EVG/TDF	INSTI	Elvitegravir	Emtricitabine/Lamivudine	TDF	Cobicistat
EVG/TAF	INSTI	Elvitegravir	Emtricitabine/Lamivudine	TAF	Cobicistat
DTG/TDF	INSTI	Dolutegravir	Emtricitabine/Lamivudine	TDF	
DTG/TAF	INSTI	Dolutegravir	Emtricitabine/Lamivudine	TAF	
DTG/ABC	INSTI	Dolutegravir	Emtricitabine/Lamivudine	Abacavir	

Abbreviations: NNRTI, non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitors; INSTI, integrase strand transfer inhibitor; TDF, tenofovir disoproxil fumarate; TAF, tenofovir alafenamide fumarate

- Change in weight was calculated as the difference in weight between baseline and subsequent visit
- We examined weight changes in both short-term (6 month) and long-term (all) follow-up using linear mixed models
  - Models were adjusted for time on regimen, the interaction between regimen and time on regimen, age, sex, race, hepatitis C and hepatitis B virus coinfection, nadir CD4, smoking, diabetes, anti-psychotic medication use (time-updated), and site
- Weight change was visually evaluated using generalized additive model (GAM) plots to assess linearity and patterns of weight change over time in both aforementioned periods after ART initiation

RESULTS

- Baseline weight was similar among all regimens
- Darunavir had the lowest average nadir CD4 count (297 cells/mm^3; DTG/TDF: 323 cells/mm^3; DTG/TAF: 364 cells/mm^3; DTG/ABC: 387 cells/mm^3; overall: 380 cells/mm^3)
- Age, sex, and race were similar among DRV, DTG/TDF, DTG/TAF, and DTG/ABC

Table 1. Short-term weight gain (6 months) comparing different ART regimens

N=2999	n	Δ kg/6 mos	95% CI		P-value
Years on regimen (EFV ref)	415	0.22	-1.00	1.45	0.72
Reg type x Years on regimen					
1: RPV	341	0.13	-1.43	1.69	0.87
2: ATV	95	2.66	0.32	5.00	0.03
3: DRV	258	4.11	2.32	5.90	0.00
4: RAL	95	2.52	0.38	4.66	0.02
5: EVG/TDF	780	2.29	0.88	3.70	0.00
6: EVG/TAF	282	2.46	0.91	4.02	0.00
7: DTG/TDF[a]	233	3.11	1.49	4.72	0.00
8: DTG/TAF[b]	116	4.88	2.17	7.59	0.00
9: DTG/ABC[c]	383	2.83	1.31	4.36	0.00

Mean number of observations per person = 3.4
[a] DTG/TDF tested different vs EFV, RPV
[b] DTG/TAF tested different vs EFV, RPV, EVG/TDF
[c] DTG/ABC tested different vs EFV, RPV

Table 2. Long-term weight gain (mean follow-up=2.0 years) comparing different ART regimens

N=2643	n	Δ kg/6 mos	95% CI		P-value
Years on regimen (EFV ref)	427	0.38	0.10	0.66	0.01
Reg type x Years on regimen*					
1: RPV	349	-0.08	-0.47	0.30	0.67
2: ATV	96	0.62	-0.20	1.44	0.14
3: DRV	263	1.07	0.53	1.61	0.00
4: RAL	99	0.55	-0.13	1.23	0.11
5: EVG/TDF	790	0.24	-0.10	0.58	0.16
7: DTG/TDF[a]	235	0.64	0.12	1.17	0.02
9: DTG/ABC[c]	383	0.75	0.37	1.14	0.00

Mean number of observations per person = 8.9
* TAF regimens not included as mean follow up time is shorter due to more recent approval
[a] DTG/TDF tested different vs EFV, RPV
[c] DTG/ABC tested different vs EFV, RPV, EVG/TDF

Figure 1. GAM plots of short-term weight gain (6 months) of select ART regimens

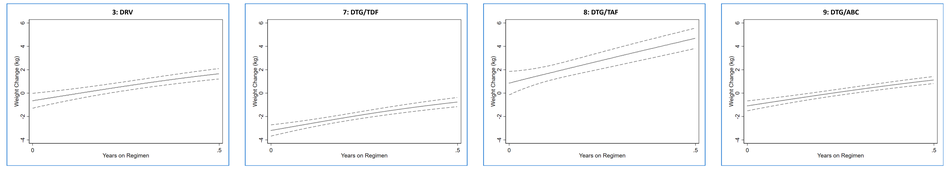
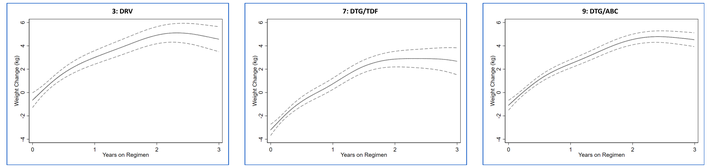


Figure 2. GAM plots of long-term weight gain (mean follow-up time=2.0 years) of select ART regimens*



* TAF regimens not included as mean follow up time is shorter due to more recent approval

LIMITATIONS

- This study had limited follow-up, which varied by each regimen, limiting comparisons of regimens over time
- ART adherence data was not included, and differential non-adherence by regimen could affect interpretation of results

STRENGTHS

- All participants were ART-naïve at baseline
- The strict regimen inclusion criteria provides clear associations
- The models incorporated anti-psychotic medication use, a known contributor to weight gain, and regimen backbone which may be particularly important in the current treatment era

CONCLUSIONS

- Dolutegravir-based regimens showed greater weight gain compared to other integrase inhibitor-based regimens in both the long- and short-term models, although the differences become smaller in the long-term
- Regimens with TAF showed greater weight gain in the first 6 months after ART initiation than the same regimen with TDF
- Darunavir showed the greatest weight gain in the long-term model, but not in short-term
- GAM plots suggest that most weight gain occurs early after ART initiation, then plateaus

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