48 months anthropometric evolution of adolescents switching to Dolutegravir in Spain

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BACKGROUND

- Dolutegravir (DTG) is now recommended as a first-line treatment for people living with HIV. However, clinical trials among adults have risen concerns regarding DTG-associated weight gain.
- The first hypothesis pointed to immune reconstitution as the underlying cause of these metabolic effects of treatment initiation, however, simplification studies demonstrated similar results.
- A clinical trial in children and adolescents has recently demonstrated the efficacy of DTG, but real-life data addressing weight gain in adolescents are still scarce.
- Childhood and adolescence are characterized by important changes in body composition, and anthropometric changes are hard to evaluate and a concern in this population, in which the impact of medication may have long lasting effects.
- We compare the anthropometric evolution of a cohort of children and adolescents who switched to DTG-based regimens vs. those who maintained their previous regimens.

METHODS

Retrospective study within the Spanish Cohort of Pediatric HIV (CORISPE). Patients < 18 years of age switching to a DTG-containing regimen before December 2020 and with at least 6 months of follow-up data were included. Patients under follow-up in the same cohort and not receiving DTG or bictegravir were included for comparison. Anthropometrics were collected every 6 months for up to 24 months of follow-up.

The WHO growth reference charts for 5 to 19 years were used to estimate zBMI. For timepoints corresponding to older age, zBMI was calculated using the 19 year old values.

Linear mixed models controlling for age, sex and ethnicity were built to model the treatment effects on zBMI over the 48 months follow-up.

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Our observational study addressing weight gain among adolescents switching to DTG shows an effect on zBMI at 12 months and maintained up to 48 months of follow-up, mainly affecting black adolescents.

RESULTS

- 275 patients were included (135 switching to DTG)
- 49% female; 48% Caucasian, 28% Black, 9% Latino.
- The median age was of 13.6 ± 2.9 years
- DTG regimens mostly included abacavir plus lamivudine (75%).
- The third drug in the control group included protease inhibitors (45%) efavirenz (32%), or elvitegravir/raltegravir (21%).
- Both groups were comparable at baseline regarding age, gender, ethnicity and zBMI.
- After controlling for age, sex, ethnicity and baseline zBMI as covariates, subjects switching to DTG experienced a greater adjusted zBMI increase than those remaining on their previous treatment (p=0.027) (**Figure 1**).

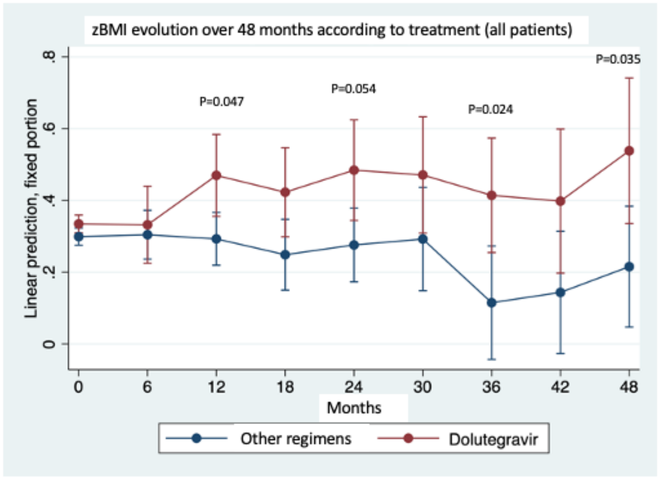

Figure 1. Z-score adjusted BMI according to treatment group in all participants
Participants receiving dolutegravir are represented using red dots and lines.
Participants receiving alternative regimens are represented in blue dots and lines. Linear mixed-models were used. Abbreviations: ART, antiretroviral treatment; zBMI z-score adjusted BMI according to WHO charts.

RESULTS

- A sub-analysis indicated that the effect on zBMI was driven by participants of black ethnicity (n=76), in which the adjusted zBMI gain was especially marked while losing significance in the non-black population (**Figure 2**).
- No differential effect was found according to sex (**Figure 3**).

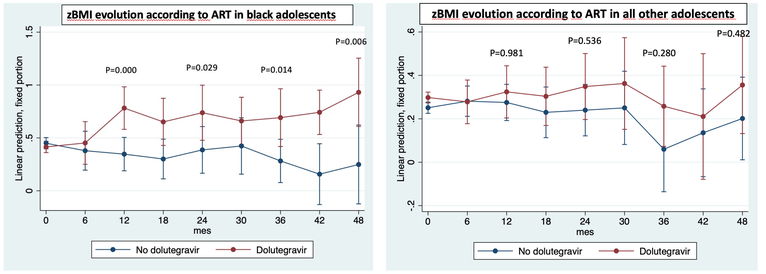

Figure 2. Z-score adjusted BMI according to treatment in black vs all other adolescents
Participants receiving dolutegravir are represented using red dots and lines.
Participants receiving alternative regimens are represented in blue dots and lines. Linear mixed-models were used. Abbreviations: ART, antiretroviral treatment; zBMI z-score adjusted BMI according to WHO.

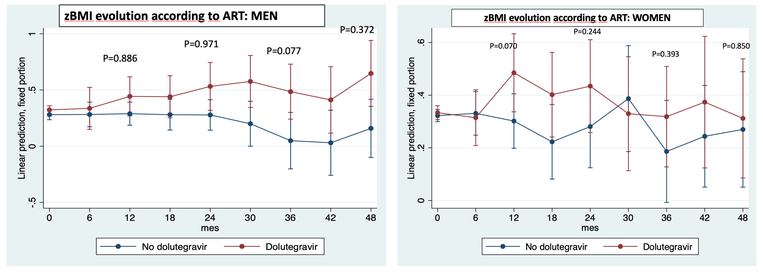

Figure 3. Z-score adjusted BMI according to treatment group in male vs female adolescents
Participants receiving dolutegravir are represented using red dots and lines.
Participants receiving alternative regimens are represented in blue dots and lines. Linear mixed-models were used. Abbreviations: ART, antiretroviral treatment; zBMI z-score adjusted BMI according to WHO.

- The prevalence of overweight remain stable over the study period (19.3% to 19.7%) while there was an increase in the prevalence of obesity (6.5% at baseline to 16.9% at 48 months) with no significant differences according to treatment group (all timepoints, p>0.05)

CONCLUSIONS

- Our observational study shows an effect of DTG switch on zBMI, already present at 12 months and maintained up to 48 months of follow-up, mainly affecting black adolescents.
- Despite the risk of residual confounders, our results are consistent with previous experience in adults suggesting a higher risk of weight gain in the black population.
- Larger studies are needed in order to analyse the long-term effects of DTG among children and adolescents, ideally including more precise assessments of body composition.