Effects of dolutegravir on growth of children and adolescents living with HIV: IeDEA global cohort

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BACKGROUND

In adults, dolutegravir (DTG)-based antiretroviral therapy (ART) has been linked with excess weight gain. However, questions remain on the impact of dolutegravir-based ART initiation on growth trajectories in children and adolescents living with HIV (CALHIV).

We examined growth trajectories, measured by BMI-for-age z-scores (zBMI), among CALHIV initiating DTG.

METHODS

Inclusion criteria for CALHIV

- Aged 1 month–19 years, from the IeDEA cohorts in West, East, Central, and Southern Africa, Asia-Pacific, Latin America and the Caribbean
- Initiated DTG from 2019 onwards
- ≥1 anthropometric measurement within 96 weeks (wks) of DTG initiation.

Statistical analyses

- Linear mixed-effects models with linear splines to compare zBMI across 3 periods (48 wks before/after DTG initiation and by 96 weeks)
- Time interaction with demographic and clinical variables to explore effect modification of zBMI trajectory and for stratification purposes.

RESULTS

Descriptive characteristics at DTG start – N=29,144

- Median age 12.8 years (Interquartile Range [IQR] 9.2–15.9)
- 54% female
- 50% from Southern Africa
- 17% ART-naïve at DTG start. Among non-ART naïve CALHIV, half transitioned from NNRTI/NRTI based regimen
- 45% had viral suppression (<50 copies/mL)
- Median zBMI –0.60 (IQR –1.44 to 0.17)
- 1.5% overweight/obese (zBMI >2)

zBMI gains and associated factors (part 1)

- Estimated mean zBMI increased by 0.13 [95%CI 0.02–0.24] in the 48 wks before DTG vs 0.19 [95%CI 0.09–0.30] in the 48 wks after, then declined to -0.02 [95%CI -0.25–0.21] by 96 wks
- No significant differences observed by sex and viral load at DTG start
- Most pronounced regional effect in West Africa (p<0.001)
- DTG+TAF regimens associated with greatest initial zBMI increase 48 wks after DTG start (+0.30 95% CI 0.18–0.49), then zBMI decrease by 96 wks (-0.08 95%CI -0.32–0.16).

After DTG initiation, children and adolescents with HIV experience modest zBMI gains that plateau by year two, suggesting a return-to-health rather than excess weight gain

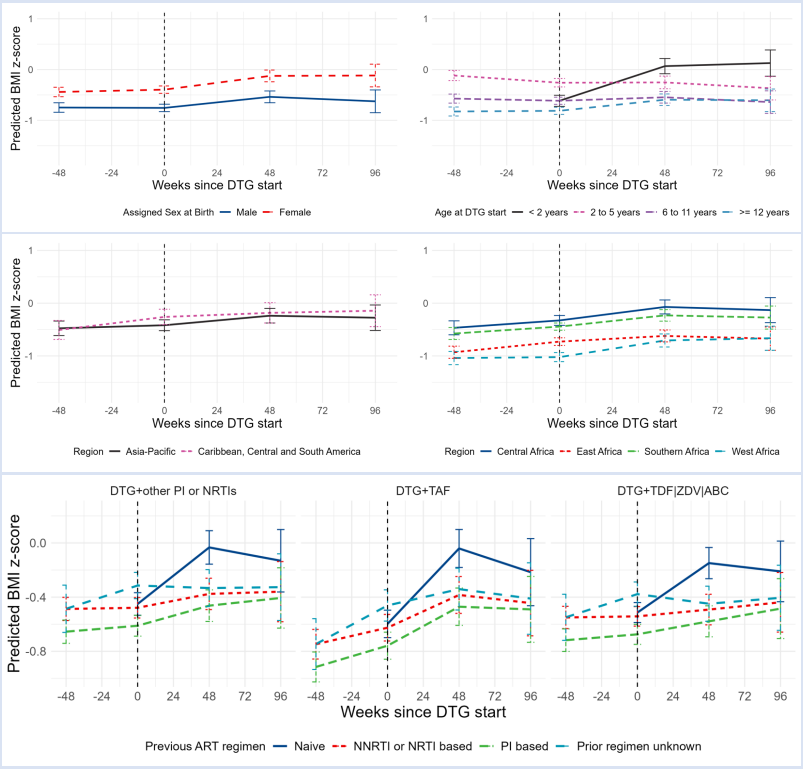


Figure 1-3. Mean BMI z-score estimated using mixed effects models with linear splines for time since DTG start, with a knot at 0 and 48 weeks, adjusted for sex, age group, region, immunological state and prior and current ART regimen composition with time interactions for each variable.
NRTI = Nucleoside/Nucleotide Reverse Transcriptase Inhibitors , NNRTI = Non-Nucleoside Reverse Transcriptase Inhibitors, PI= Protease Inhibitors (PIs), DTG = dolutegravir, TAF = Tenofovir Alafenamide, TDF = Tenofovir disoproxil fumarate, ZDV = Zidovudine, ABC = Abacavir

RESULTS

zBMI gains and associated factors (part 2)

- ART-naïve CALHIV starting DTG with TAF had the steepest initial gain (48 wks before: 0.16 [95%CI -0.13–0.43] vs 48 wks after: 0.56 [95%CI 0.44–0.68], p=0.017), followed by a decline (by 96 wks -0.16 [95%CI –0.41–0.08]), compared to naïve or non-naïve CALHIV starting with other NRTIS.

CONCLUSIONS

In this large global cohort of children and adolescents living with HIV, DTG initiation was associated with modest increases in zBMI. These gains were slightly more pronounced among those receiving DTG+TAF or with poorer immunological status at baseline, but generally plateaued or declined by year two of follow-up. This trajectory is consistent with a "return-to-health" effect rather than sustained excess weight gain. Overall, these findings support the continued use of DTG in CALHIV, while emphasizing the importance of ongoing monitoring in specific subgroups and the need for further research into long-term metabolic outcomes.

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PLAIN LANGUAGE SUMMARY

After starting dolutegravir, children and adolescents with HIV gained a small amount of weight that stabilized over time, consistent with improved health.