Weight Change and Metabolic Assessment of Virologically Suppressed Children With HIV Aged ≥ 2 Years and Weighing 14 to < 25 Kg Who Received a TAF-Containing Regimen

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Key Findings

In children with virologic suppression of HIV aged ≥ 2 years and weighing 14 to < 25 kg:

- Weight, height and body mass index (BMI) increased from baseline to Week 48, consistent with growth expectations for age
- At Week 48, the proportion of participants who were underweight decreased and the proportion who had normal weight increased
  - The proportion of participants who were overweight or obese remained stable
- Baseline factors associated with greater change in BMI-for-age percentile at Week 48 were being underweight and being female
- The proportions of participants with acceptable levels of total cholesterol, low-density lipoprotein (LDL) cholesterol and triglycerides increased from baseline to Week 48

Conclusions

- Observed changes in weight, height and BMI after switching to a TAF-based regimen are consistent with child development in this age group
- Overall, lipid metabolism parameters improved during 48 weeks of treatment

Introduction

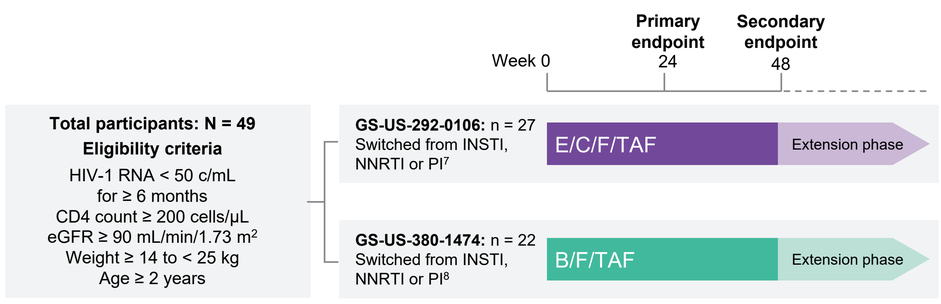
- Weight gain has been noted in adolescents living with HIV switching to integrase strand transfer inhibitor–based regimens, although weight remains in the normal range for age[1,2]
- In adults, some antiretroviral therapies (ARTs), including TDF, are associated with reversible weight suppression[3–5]
- TAF-based regimens are being used more widely in pediatric populations
- Previous data in children and adolescents aged 6 to < 18 years switching to TAF showed weight changes consistent with expected weight dynamics for this age group[6]

Objective

- To investigate the impact of switching to a TAF-based regimen on weight, BMI and lipid parameters over 48 weeks of treatment in children living with HIV who are aged ≥ 2 years and weigh 14 to < 25 kg

Methods

Studies Included in the Pooled Analysis



Demographics and changes from baseline to Week 48 in weight, height, BMI and lipid metabolism parameters were evaluated

eGFR was calculated using the Schwartz formula. c, copies; CD, cluster of differentiation; eGFR, estimated glomerular filtration rate; INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

Statistical Analysis

- Descriptive analyses were performed on pooled data from children living with HIV aged ≥ 2 years and weighing 14 to < 25 kg who received ≥ 1 dose of either study drug
- Univariate linear regression analysis was conducted to investigate baseline characteristics associated with BMI-for-age percentile change from baseline to Week 48
  - A list of possible independent variables as predictors or adjustment variables was devised based on expert clinical opinion
  - The independent variables were used for variable selection in a multiple linear regression model using a stepwise regression approach
- Z-scores and percentiles were generated based on year 2000 growth charts from the U.S. Centers for Disease Control and Prevention (CDC) website[9]

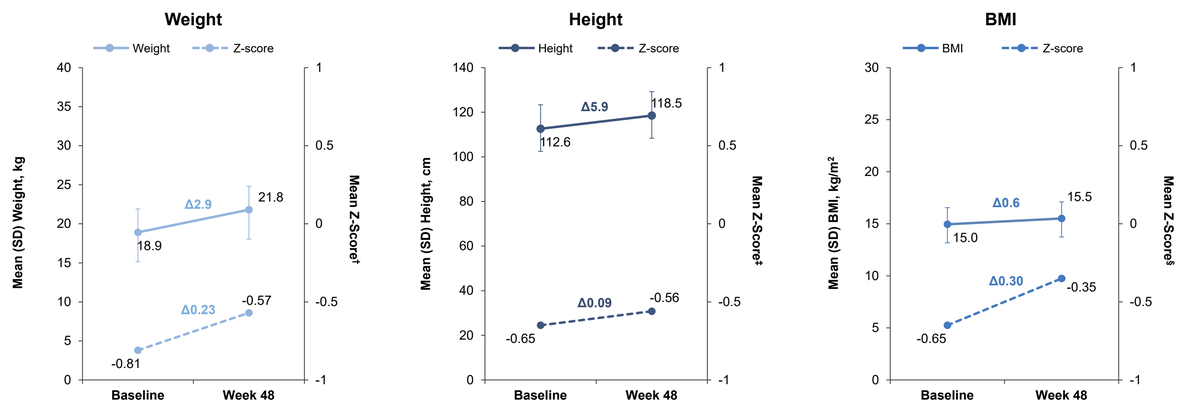
Results

Demographic and Baseline Characteristics (N = 49)

Characteristic		E/C/F/TAF n = 27	B/F/TAF n = 22	Total N = 49
Age, years, median (Q1, Q3)		6 (4, 8)	6 (3, 7)	6 (4, 7)
Female at birth, n (%)		17 (63.0)	11 (50.0)	28 (57.1)
Race, n (%)	Black	24 (88.9)	16 (72.7)	40 (81.6)
	Asian	3 (11.1)	5 (22.7)	8 (16.3)
CD4 count/μL, median (Q1, Q3)		1,061 (895, 1,315)	962 (748, 1,419)	1,020 (879, 1,351)
CD4 %, median (Q1, Q3)		37.4 (30.6, 40.3)	32.0 (29.3, 37.2)	34.7 (30.6, 39.2)
Baseline NRTI, n (%)	TDF	1 (3.7)	0	1 (2.0)
	Non-TAF/TDF	26 (96.3)	22 (100)	48 (98.0)
Prior NRTI, n (%)		27 (100)	22 (100)	49 (100)
3TC		24 (88.9)	17 (77.3)	41 (83.7)
ABC		20 (74.1)	18 (81.8)	38 (77.5)
Non-ABC		7 (25.9)	5 (22.7)	12 (24.5)
Prior EFV, n (%)		3 (11.1)	9 (40.9)	12 (24.5)

3TC, lamivudine; ABC, abacavir; EFV, efavirenz; NRTI, nucleos(t)ide reverse transcriptase inhibitor; Q, quartile.

Weight, Height and BMI at Baseline, and Changes at Week 48*: Total Population (N = 49)

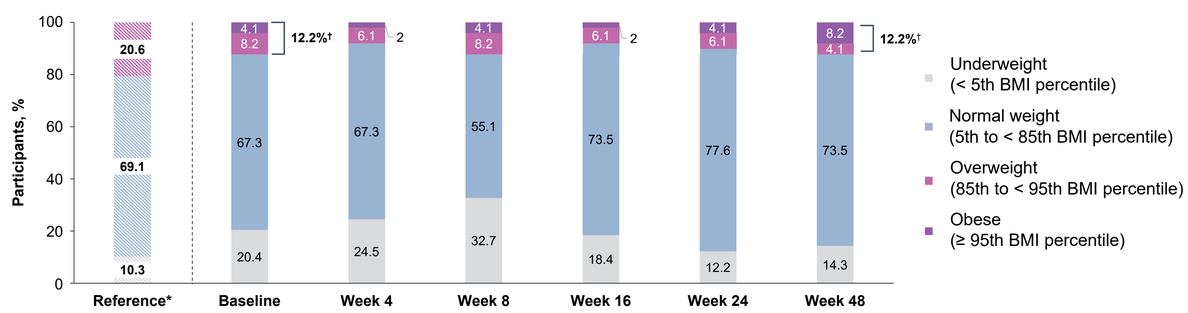


*Z-scores and percentiles were generated based on year 2000 growth charts from the CDC, calculated for child's sex and age[9]; †SD for weight z-score was 1.05 kg at baseline and 1.11 kg at Week 48; ‡SD for height z-score was 1.10 cm at baseline and 1.20 cm at Week 48; §SD for BMI z-score was 1.26 kg/m² at baseline and 1.22 kg/m² at Week 48. SD, standard deviation.

BMI-for-age percentile increased from baseline to Week 48 by 6.8%

- Z-scores for weight, height and BMI all increased

BMI Categories by Visit: Total Population (N = 49)



*Reference WHO global prevalence data are shown for children aged 5–9 years: underweight, < -2 SD below the median; overweight/obese, > 1 SD above the median.[10] †Numbers may not appear to sum to 100% due to rounding. BMI categories for study data are according to CDC growth charts.[9,11] WHO, World Health Organization.

- At Week 48, the proportion of participants who were underweight decreased and the proportion with normal weight increased compared with baseline; the proportion who were overweight or obese remained stable

For the results by individual study, please scan the QR code

Predictors of Change in BMI-for-Age Percentile at Week 48: Univariate Linear Regression Analysis (N = 49)

Explanatory variable	Test vs. reference	Estimate (95% CI)	*P*-value
Age (years)	Continuous	1.0 (-1.7, 3.6)	0.4700
Sex at birth	**Female** vs. male (ref.)	8.1 (-1.5, 17.7)	0.0978
Race	**Black** vs. non-Black (ref.)	9.2 (-3.2, 21.6)	0.1407
Baseline ABC	**Yes** vs. no (ref.)	5.8 (-4.9, 16.5)	0.2787
Baseline EFV	**Yes** vs. no (ref.)	-6.2 (-17.5, 5.0)	0.2694
Current regimen	**E/C/F/TAF** vs. B/F/TAF (ref.)	4.8 (-5.0, 14.5)	0.3305
BMI category at baseline	**Underweight** vs. overweight/obese (ref.)	17.4 (0.2, 34.5)	0.0471
BMI category at baseline	**Normal** vs. overweight/obese (ref.)	9.3 (-5.4, 24.0)	0.2090

*According to CDC growth charts.[9,11] CI, confidence interval; ref., reference.

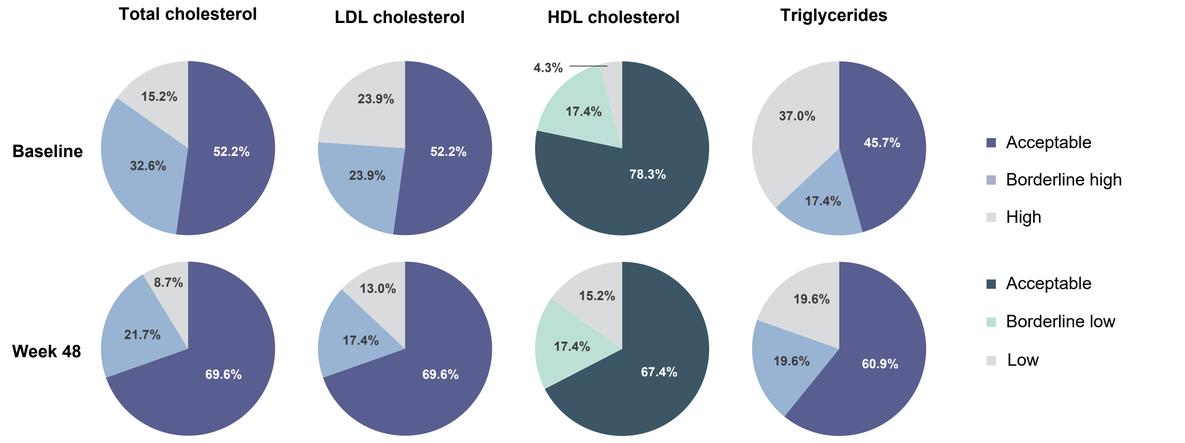
- An additional analysis using a stepwise multivariate regression approach was then performed on the above variables, resulting in a final model containing the predictors of sex at birth, baseline ABC, and BMI category at baseline ($P < 0.15$)

For final model analyses, please scan the QR code

Proportion of Participants With Acceptable Lipid Levels: Total Population (N = 46)

- Proportions of participants with acceptable levels of total cholesterol, LDL cholesterol and triglycerides increased from baseline to Week 48
  - Proportion of participants with low high-density lipoprotein (HDL) cholesterol increased from baseline to Week 48

For median lipid values and results by individual study, please scan the QR code



Categories were based on integrated guidelines for cardiovascular health and risk reduction in children and adolescents.[12]
Due to rounding, percentages may not total 100%.

References: **1.** Dirajlal-Fargo S, et al. CROI 2020, Abstract 826. **2.** Turkova A, et al. IAS 2021, Abstract 1311. **3.** Erlandson KM, et al. Clin Infect Dis 2021;73:1440-1451. **4.** Cahn P, et al. IAS 2019, Oral WEAB0404LB. **5.** Mallon PWG, et al. J Int AIDS Soc 2021;24:e25702. **6.** Rakhmanina N, et al. Int Pediatr Workshop 2020, Poster 56. **7.** NCT01854775. https://clinicaltrials.gov/ct2/show/NCT01854775 (accessed May 24, 2023). **8.** NCT02881320. https://clinicaltrials.gov/ct2/show/NCT02881320 (accessed May 24, 2023). **9.** CDC. https://www.cdc.gov/nchs/data/series/sr_11/sr11_246.pdf (accessed May 24, 2023). **10.** WHO. https://www.who.int/data/gho/data/indicators (accessed May 24, 2023). **11.** CDC. https://www.cdc.gov/obesity/basics/childhood-defining.html (accessed May 24, 2023). **12.** Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction In Children and Adolescents. Pediatrics 2011;128(Suppl. 5):S213-S256.

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Abbreviations: 3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BMI, body mass index; c, copies; CD, cluster of differentiation; CDC, Centers for Disease Control and Prevention; CI, confidence interval; E/C/F/TAF, elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide; EFV, efavirenz; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; INSTI, integrase strand transfer inhibitor; LDL, low-density lipoprotein; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleos(t)ide reverse transcriptase inhibitor; PI, protease inhibitor; Q, quartile; ref., reference; SD, standard deviation; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; WHO, World Health Organization.

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