Efficacy and Safety of Emtricitabine/Tenofovir Alafenamide (F/TAF) Plus Cobicistat-Boosted Protease Inhibitors in Children With HIV-1 Aged 2 to < 12 Years and Weighing 14 to < 40 kg: Week 48 Outcomes

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Conclusions

- In this Week 48 analysis in children with HIV aged 2 to < 12 years and weighing ≥ 14 to < 40 kg, emtricitabine/tenofovir alafenamide (F/TAF) in combination with cobicistat-boosted atazanavir (ATV/c) or cobicistat-boosted darunavir (DRV/c) demonstrated favorable efficacy, safety, and acceptability
- All participants with available data maintained or achieved virologic suppression through 48 weeks of treatment
- F/TAF in combination with ATV/c or DRV/c was well tolerated
  - There were no renal, bone, or weight gain/loss concerns
- Most participants/caregivers reported that the tablets were of an acceptable shape and size
- These data support further evaluation of F/TAF in combination with ATV/c or DRV/c in children with HIV

Plain Language Summary

- F/TAF is a single tablet used to treat people with human immunodeficiency virus (HIV)
  - It contains two different medicines: emtricitabine (F) and tenofovir alafenamide (TAF), and is normally taken with a third HIV medicine
- F/TAF is approved to be used together with HIV medicines called boosted protease inhibitors in older children, including teenagers, who weigh at least 35 kg (77 lb)
  - Studies in children aged 2 years and older are now being done
- In this study, children aged 2 years and older and weighing at least 14 kg (31 lb) were taking F/TAF together with either cobicistat-boosted atazanavir (ATV/c) or cobicistat-boosted darunavir (DRV/c)
  - ATV/c and DRV/c are HIV medicines called boosted protease inhibitors
  - Cobicistat helps to raise ('boost') the levels of ATV and DRV in the blood to make them work better
- This poster reports results after 48 weeks, showing how well the medicines are working, if there are any new side effects, and how easy the tablets are to take
- After 48 weeks, F/TAF taken together with ATV/c or DRV/c worked well at controlling the amount of HIV in the blood
- No new side effects were seen, and the tablets were easy to take

Introduction

- Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) in combination with boosted protease inhibitors (PIs) are guideline-recommended regimens for the treatment of HIV-1 in children with intolerability or resistance to integrase strand transfer inhibitors[1]
- F/TAF is a dual NRTI approved in the US in combination with boosted PIs for adults and for children and adolescents weighing ≥ 35 kg, and with other antiretroviral therapies (ARTs) for children weighing ≥ 14 kg.[1,2,a] In the European Union, F/TAF is approved in combination with other ARTs, including boosted PIs, for adults and adolescents aged ≥ 12 years and weighing ≥ 35 kg[3,b]
  - TAF is associated with improved renal and bone safety compared with tenofovir disoproxil fumarate[4]
  - Cobicistat is a pharmacokinetic enhancer with no antiretroviral activity that can be easily coformulated with other ARTs[5]
- In the pediatric population, safety and efficacy data are limited for cobicistat-boosted PIs, including boosted PIs in combination with F/TAF
- GS-US-216-0128 (NCT02016924) is an ongoing Phase 2/3, multicenter, open-label, multicohort trial evaluating F/TAF and boosted PIs in children and adolescents with HIV-1

[a]In the US, the recommended dose of F/TAF for adults, adolescents, and children weighing ≥ 35 kg is 200/25 mg once daily, regardless of whether they are receiving a boosted PI; the recommended dose for children and adolescents not receiving a boosted PI is 200/25 mg once daily for those weighing ≥ 25 to < 35 kg and 120/15 mg once daily for those weighing ≥ 14 to < 25 kg.[2] [b]In the European Union, the recommended dose of F/TAF for adults, adolescents, and children weighing ≥ 35 kg is 200/25 mg once daily for those not receiving a boosted PI and 200/10 mg for those receiving a boosted PI.[3]

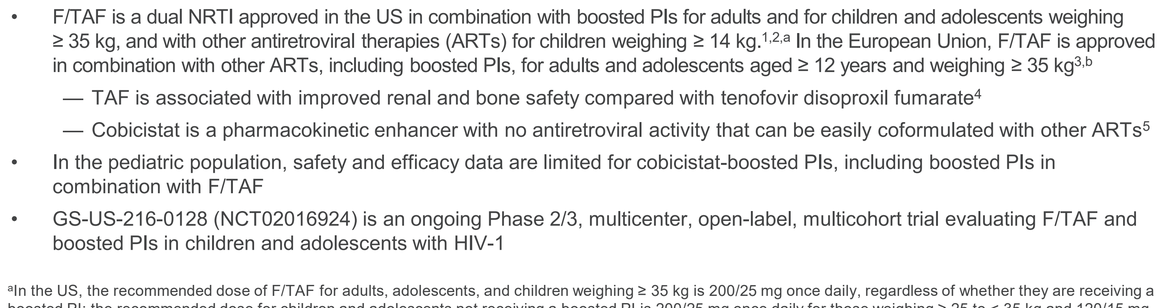
Objective

- To evaluate the efficacy and safety of F/TAF in combination with ATV/c or DRV/c in children with HIV-1 aged 2 to < 12 years, weighing ≥ 14 to < 40 kg at screening, from Cohorts 2 and 3 of Study GS-US-216-0128 (NCT02016924), through Week 48

Methods

Study Design

- This analysis focused on participants who were aged 6 to < 12 years weighing ≥ 25 to < 40 kg (Cohort 2), and aged ≥ 2 years weighing ≥ 14 to < 25 kg (Cohort 3)



Enrollment: [a]South Africa n = 8, Zimbabwe n = 6; [b]South Africa n = 3, Zimbabwe n = 5, USA n = 1; [c]South Africa n = 10, Zimbabwe n = 5; [d]South Africa n = 7, Zimbabwe n = 4. [e]Data review by the IDMC occurred after the last participant was enrolled in each cohort and ≥ 50% of participants had completed Week 12. [f]All participants weighing ≥ 35 kg received DRV; cobicistat dose was 150 mg; ATV and DRV were dosed by weight. [g]Participants must have been aged ≥ 3 years and ≥ 15 kg to receive DRV; cobicistat was a 90-mg low-dose tablet; ATV and DRV were dosed by weight. [h]Cumulative through data-cut (when the last participant enrolled in Cohorts 2 and 3 had completed Week 48). ATV, atazanavir; c, cobicistat; CD4, cluster of differentiation 4; DRV, darunavir; eGFR, estimated glomerular filtration rate by Schwartz formula; F/TAF, emtricitabine/tenofovir alafenamide; FDA, (US) Food and Drug Administration; IDMC, Independent Data Monitoring Committee; iPK, intensive pharmacokinetics; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor.

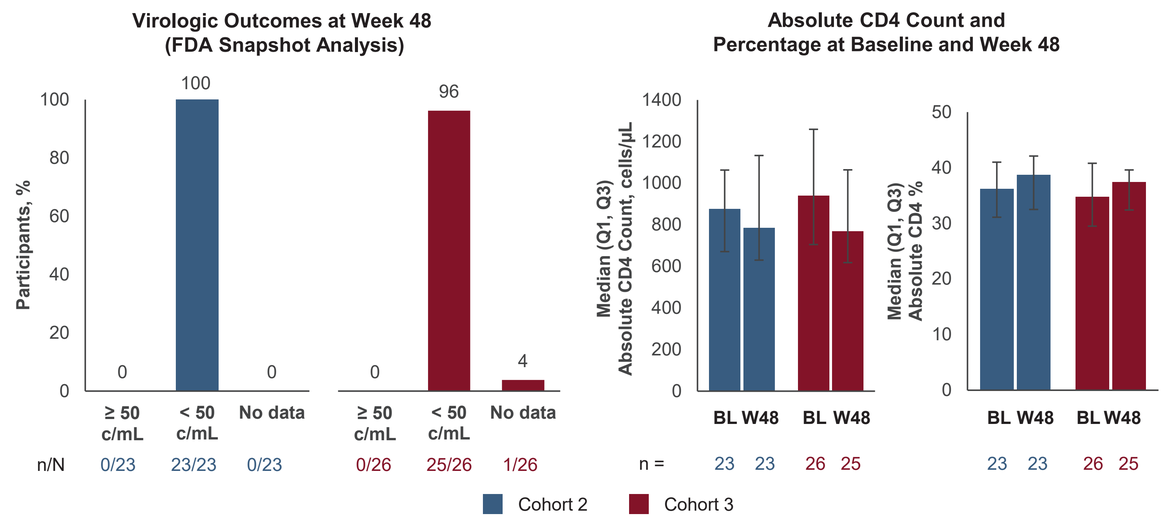
Results

Baseline Demographics and Disease Characteristics

	Cohort 2 (6 to < 12 years; ≥ 25 to < 40 kg) n = 23	Cohort 3 (≥ 2 years; ≥ 14 to < 25 kg) n = 26
Age, years, median (range)	10 (8-12)	6 (3-10)
Female sex at birth, n (%)	14 (61)	14 (54)
Race, n (%)		
Black	21 (91)	24 (92)
Other	2[a] (9)	2[b] (8)
Hispanic or Latine ethnicity,[c] n/N (%)	1/22 (5)	1/25 (4)
HIV-1 RNA < 50 c/mL, n (%)	22 (96)	24 (92)
CD4 count, cells/μL, median (Q1, Q3)	876 (671, 1063)	940 (705, 1259)
CD4, %, median (Q1, Q3)	36.2 (31.1, 41.0)	34.8 (29.5, 40.8)
Vertical transmission, n (%)	22[d] (96)	26 (100)
Asymptomatic disease status, n (%)	22 (96)	26 (100)

[a]One participant was of mixed race (Black/White) and one participant did not want to report their race. [b]Both participants were of mixed race (Black/White). [c]Data were unavailable for one participant in each cohort. [d]Mode of transmission was unknown for one participant. c, copies; CD4, cluster of differentiation 4; Q, quartile.

Efficacy Outcomes at Week 48



Cohort 2: 6 to < 12 years; ≥ 25 to < 40 kg; Cohort 3: ≥ 2 years; ≥ 14 to < 25 kg. BL, baseline; c, copies; CD4, cluster of differentiation 4; FDA, (US) Food and Drug Administration; Q, quartile; W, Week.

- All participants with available data maintained or achieved virologic suppression at Week 48
- Absolute CD4 count and percentage remained within the expected range of physiological fluctuation for this age group

Cumulative Safety Outcomes

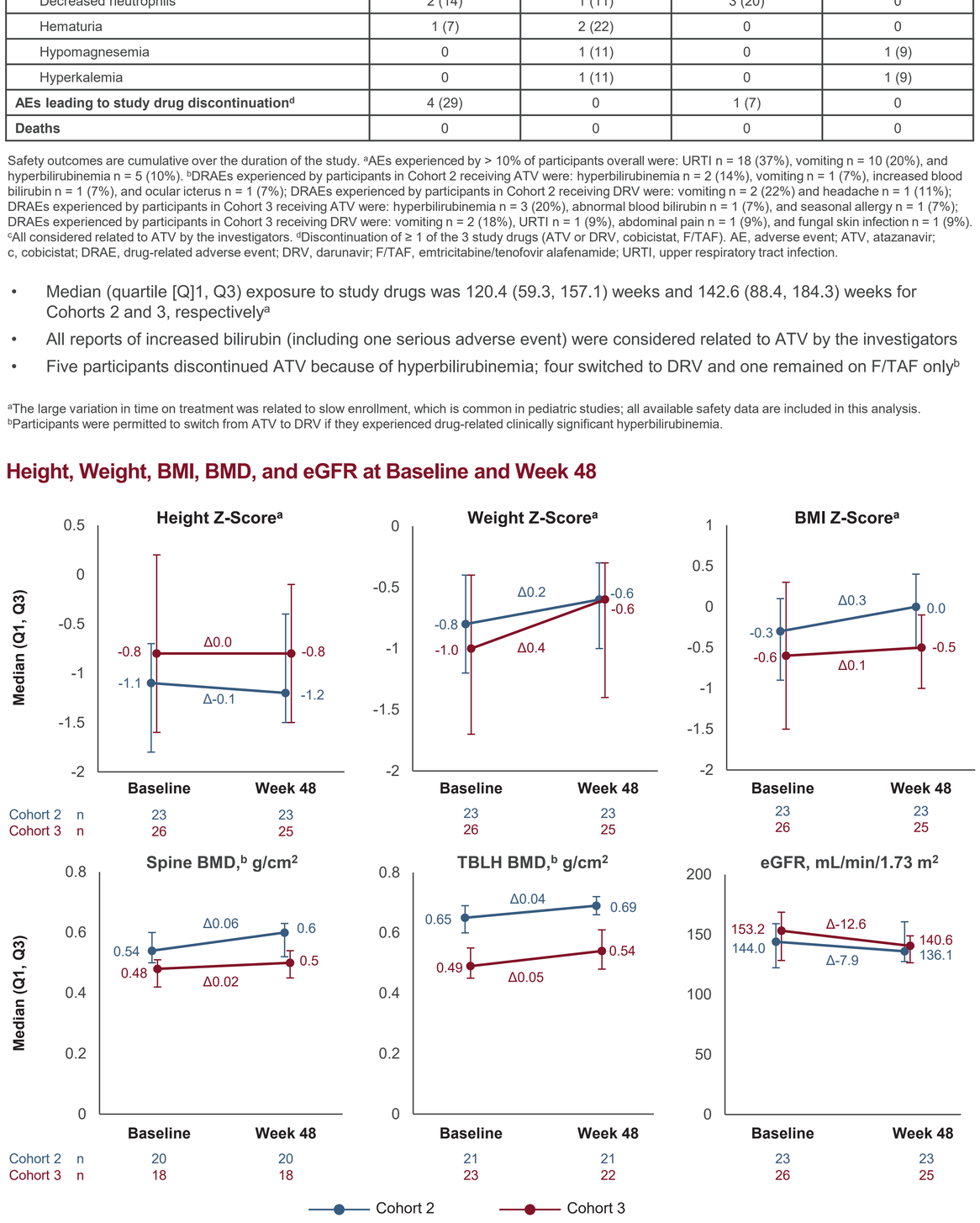
n (%)	Cohort 2 (6 to < 12 years; ≥ 25 to < 40 kg) n = 23		Cohort 3 (≥ 2 years; ≥ 14 to < 25 kg) n = 26	
	ATV/c + F/TAF n = 14	DRV/c + F/TAF n = 9	ATV/c + F/TAF n = 15	DRV/c + F/TAF n = 11
Any AE[a]	12 (86)	8 (89)	12 (80)	11 (100)
DRAEs[b]	4 (29)	3 (33)	4 (27)	3 (27)
Grade 3/4 DRAEs	0	0	2 (13)	0
Increased bilirubin/hyperbilirubinemia[c]	0	0	2 (13)	0
Serious DRAEs	0	0	1 (7)	0
Hyperbilirubinemia[c]	0	0	1 (7)	0
Grade 3/4 laboratory abnormalities affecting ≥ 2 participants overall				
Hyperbilirubinemia	7 (50)	0	7 (47)	0
Increased amylase	4 (29)	1 (11)	3 (20)	1 (9)
Decreased neutrophils	2 (14)	1 (11)	3 (20)	0
Hematuria	1 (7)	2 (22)	0	0
Hypomagnesemia	0	1 (11)	0	1 (9)
Hyperkalemia	0	1 (11)	0	1 (9)
AEs leading to study drug discontinuation[d]	4 (29)	0	1 (7)	0
Deaths	0	0	0	0

Safety outcomes are cumulative over the duration of the study. [a]AEs experienced by > 10% of participants overall were: URTI n = 18 (37%), vomiting n = 10 (20%), and hyperbilirubinemia n = 5 (10%). [b]DRAEs experienced by participants in Cohort 2 receiving ATV were: hyperbilirubinemia n = 2 (14%), vomiting n = 1 (7%), increased blood bilirubin n = 1 (7%), and ocular icterus n = 1 (7%); DRAEs experienced by participants in Cohort 2 receiving DRV were: vomiting n = 2 (22%) and headache n = 1 (11%); DRAEs experienced by participants in Cohort 3 receiving ATV were: hyperbilirubinemia n = 3 (20%), abnormal blood bilirubin n = 1 (7%), and seasonal allergy n = 1 (7%); DRAEs experienced by participants in Cohort 3 receiving DRV were: vomiting n = 2 (18%), URTI n = 1 (9%), abdominal pain n = 1 (9%), and fungal skin infection n = 1 (9%). [c]All considered related to ATV by the investigators. [d]Discontinuation of ≥ 1 of the 3 study drugs (ATV or DRV, cobicistat, F/TAF). AE, adverse event; ATV, atazanavir; c, cobicistat; DRAE, drug-related adverse event; DRV, darunavir; F/TAF, emtricitabine/tenofovir alafenamide; URTI, upper respiratory tract infection.

- Median (quartile [Q]1, Q3) exposure to study drugs was 120.4 (59.3, 157.1) weeks and 142.6 (88.4, 184.3) weeks for Cohorts 2 and 3, respectively[a]
- All reports of increased bilirubin (including one serious adverse event) were considered related to ATV by the investigators
- Five participants discontinued ATV because of hyperbilirubinemia; four switched to DRV and one remained on F/TAF only[b]

[a]The large variation in time on treatment was related to slow enrollment, which is common in pediatric studies; all available safety data are included in this analysis. [b]Participants were permitted to switch from ATV to DRV if they experienced drug-related clinically significant hyperbilirubinemia.

Height, Weight, BMI, BMD, and eGFR at Baseline and Week 48



Cohort 2: 6 to < 12 years; ≥ 25 to < 40 kg; Cohort 3: ≥ 2 years; ≥ 14 to < 25 kg. Baseline values were the last available values collected on/before first dose of study drug. [a]Z-scores generated using 2000 US Centers for Disease Control and Prevention Growth Charts.[6] [b]BMD assessed using dual-energy X-ray absorptiometry of spine and TBLH. BMD, bone mineral density; BMI, body mass index; eGFR, estimated glomerular filtration rate by Schwartz formula; Q, quartile; TBLH, total body less head.

- There were no clinically significant changes in height, weight, body mass index, bone mineral density or estimated glomerular filtration rate from baseline to Week 48

Acceptability

Cohort 2: 6 to < 12 years; ≥ 25 to < 40 kg; Cohort 3: ≥ 2 years; ≥ 14 to < 25 kg. Denominator for percentage is based on the non-missing data at each visit. [a]In Cohort 2, acceptability (size and shape) was not assessed separately for F/TAF and cobicistat. F/TAF, emtricitabine/tenofovir alafenamide.

- Most participants/caregivers reported that the tablets had a favorable size and shape

References: **1.** Department of Health and Human Services. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/pediatric-arv/guidelines-pediatric-arv.pdf (accessed Apr. 23, 2025). **2.** Descovy USPI, Gilead Sciences, January 2022. **3.** Descovy SmPC, Gilead Sciences, February 2023. **4.** DeJesus E, et al. *AIDS Res Hum Retroviruses.* 2018;34:337-42. **5.** Clinicalinfo.HIV.gov. https://clinicalinfo.hiv.gov/en/drugs/cobicistat/patient (accessed Apr. 23, 2025). **6.** Kuczmarski RJ, et al. *Vital Health Stat.* 2002;11:1-190.

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