Longitudinal Lymphocyte Dynamics in Virologically Suppressed Children With HIV Initiating Single-Tablet Elvitegravir, Cobicistat, Emtricitabine and Tenofovir Alafenamide (E/C/F/TAF)

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Key Findings

- At baseline, absolute lymphocyte count and cluster of differentiation (CD) 4 and CD8 T-cell subpopulation counts were higher in the younger cohort (aged ≥ 2 years, weight 14 to < 25 kg; Cohort 3) than in the older cohort (6 to < 12 years, ≥ 25 kg; Cohort 2)
  - These observations are consistent with finding in children without HIV
- Absolute lymphocyte counts declined over 48 weeks of treatment with E/C/F/TAF within the expected range for this age population
- Absolute CD4 T-cell counts decreased from baseline to Week 48 in both cohorts, with larger decreases seen in the younger Cohort 3
  - These results are consistent with the physiological decline observed with age in populations without HIV
- CD4/CD8 ratio and CD4 T-cell percentage remained stable during treatment with E/C/F/TAF

Conclusions

- Lymphocyte dynamics change with age, and age-specific reference ranges should be used to support clinical decision-making based on lymphocyte counts and distributions in children living with HIV
- Absolute lymphocyte and subset panel counts (including CD4 T-cell counts) in children living with HIV who remained in virologic suppression on E/C/F/TAF for 48 weeks were within age-specific reference ranges, in line with the changes seen in children without HIV
- No clinically relevant effects of E/C/F/TAF on lymphocytes were identified in this population

Introduction

- Total lymphocyte counts decrease with age from birth to adolescence, as demonstrated in children aged 0 to 18 years without HIV in Uganda and in an urban area of minority predominance in the U.S.A.[1,2]
- Some antiretroviral treatment (ART) regimens have been associated with effects on hematologic parameters, including in pediatric populations[3,4]

Objective

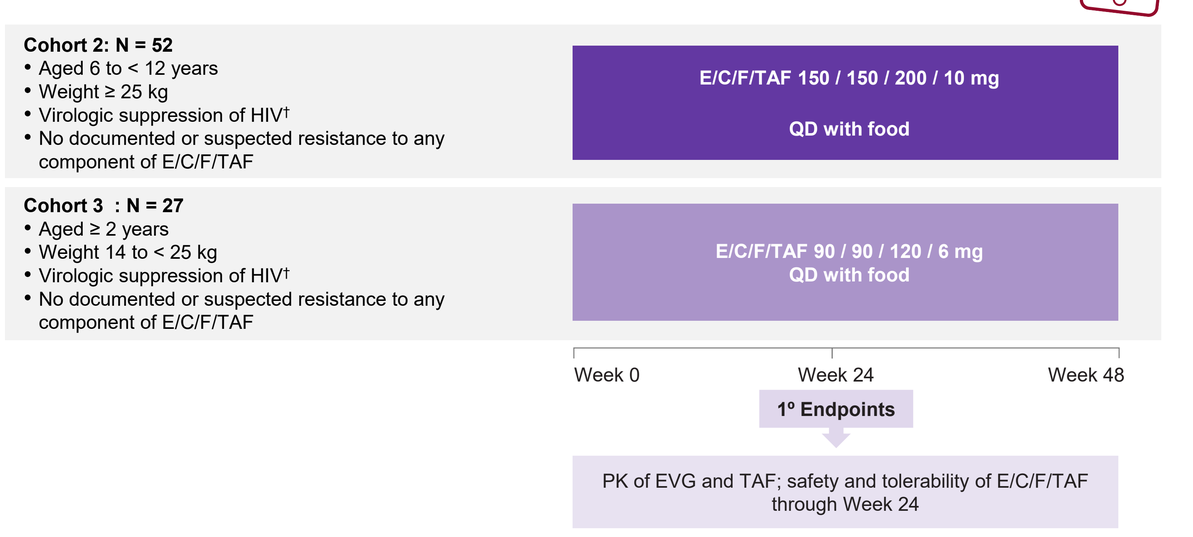
- To assess **lymphocyte dynamics** in **children with virologic suppression of HIV** (aged 2 to < 12 years) receiving E/C/F/TAF once daily (QD) for 48 weeks

Methods

- This analysis included children with virologic suppression of HIV from two cohorts (Cohorts 2 and 3) of a Phase 2/3 open-label study[5] (NCT01854775) investigating the pharmacokinetics (PK), safety and antiviral activity of E/C/F/TAF
- Children in Cohort 2 (aged 6 to < 12 years, weight ≥ 25 kg) and Cohort 3 (≥ 2 years, 14 to < 25 kg) received E/C/F/TAF QD for ≥ 48 weeks
- Absolute counts and percentages of CD4 and CD8 T cells, B cells and natural killer (NK) cells from total lymphocytes were evaluated by flow cytometry of whole blood

Study Design[5]

For further details of the methods, please scan the QR code



Participants in Cohort 2 (N = 52): Thailand n = 13, Uganda n = 27, U.S.A. n = 12; Cohort 3 (N = 27): South Africa n = 13, Thailand n = 1, Uganda n = 8, U.S.A. n = 3, Zimbabwe n = 2. *These 50 participants received the same study drug schedule as Cohort 2, but are not included in this analysis; †Plasma HIV-1 RNA < 50 copies/mL for ≥ 180 consecutive days before screening on a stable ART regimen

Results

Demographics and Baseline Characteristics

Characteristic		≥ 2 years* (Cohort 3) N = 27	6 to < 12 years† (Cohort 2) N = 52
Age, years, median (range)		6 (3–9)	10 (7–11)
Age group, n (%)	2–5 years 6–12 years	11 (41) 16 (59)	– 52 (100)
Male, n (%)		10 (37)	22 (42)
Race, n (%)	Black Asian White	24 (89) 3 (11) 0	37 (71) 13 (25) 2 (4)
Ethnicity – not Hispanic or Latinx, n (%)		27 (100)	52 (100)
Weight, kg, median (Q1, Q3)		19.3 (17.0, 20.5)	30.9 (28.1, 33.7)
Weight, z-score, median (Q1, Q3)		-0.88 (-1.72, -0.32)	-0.48 (-1.01, 0.14)
Height, z-score, median (Q1, Q3)		-0.28 (-1.42, 0.23)	-0.73 (-1.26, 0.10)
CD4 T-cell %, median (Q1, Q3)		37.4 (30.6, 40.3)	38.7 (33.9, 43.0)
CD4 T-cell count, cells/µL, median (Q1, Q3)		1,061 (897, 1,315)	933 (765, 1,100)

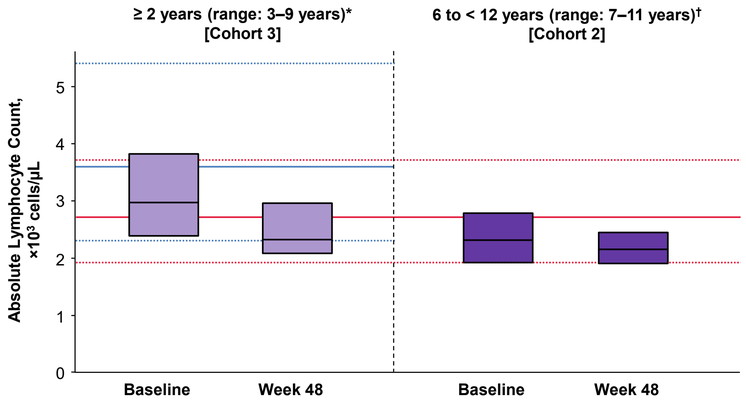
*Weight 14 to < 25 kg; †Weight ≥ 25 kg. Q, quartile.

Lymphocyte Subsets at Baseline and Week 48

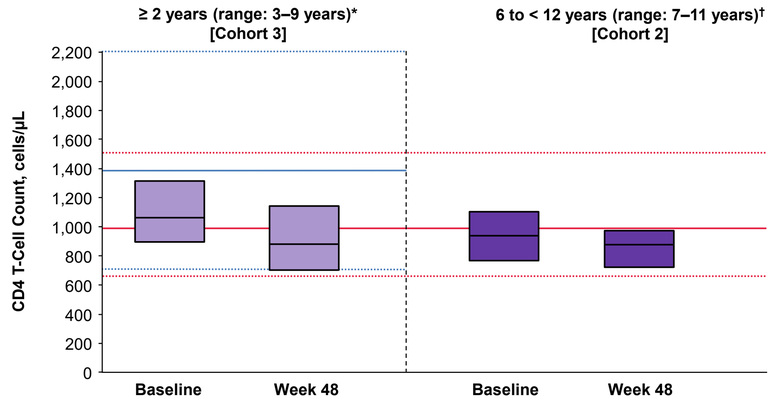
	≥ 2 years* (Cohort 3) N = 27		6 to < 12 years† (Cohort 2) N = 52		Reference values‡	
	Baseline	Week 48	Baseline	Week 48	≥ 2 to < 6 years	≥ 6 to < 12 years
Absolute lymphocyte cell count/µL	2,960 (2,390, 3,820)	2,320 (2,080, 2,970)‡	2,310 (1,920, 2,780)	2,150 (1,900, 2,440)§	3,600 (2,300, 5,400)	2,700 (1,900, 3,700)
CD4 T-cell (CD3+/CD4+) count/µL	1,061 (897, 1,315)	883 (702, 1,144)	933 (765, 1,100)	872 (720, 969)	1,380 (700, 2,200)	980 (650, 1,500)
CD8 T-cell (CD3+/CD8+) count/µL	870 (705, 1,168)	832 (683, 1,023)	790 (653, 928)	714 (544, 867)	840 (490, 1,300)	680 (370, 1,100)
B-cell (CD3-/CD19+) count/µL	584 (300, 862)	435 (337, 577)	323 (201, 414)	323 (250, 431)	670 (20, 1,400)	340 (0, 740)
NK-cell (CD3-/CD16+/CD56+) count/µL	213 (177, 365)	265 (180, 403)	188 (123, 257)	251 (130, 359)	300 (130, 720)	230 (100, 480)

Data are median (Q1, Q3) for Cohorts 2 and 3, and median (10th percentile, 90th percentile) for reference values. Participant age ranges were 3–9 years (Cohort 3) and 7–11 years (Cohort 2). *Weight 14 to < 25 kg; †Weight ≥ 25 kg; ‡n = 25; §n = 51.

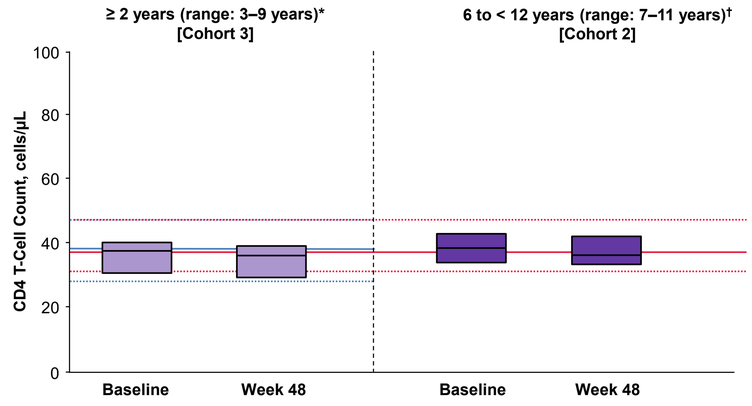
Absolute Lymphocyte Count at Baseline and Week 48



CD4 T-Cell Count at Baseline and Week 48



CD4 T-Cell Percentage at Baseline and Week 48



Box plots represent Q1, median and Q3 values. *Weight 14 to < 25 kg; †Weight ≥ 25 kg

CD4/CD8 T-Cell Ratio at Baseline and Week 48

- CD4/CD8 ratio remained stable during treatment with E/C/F/TAF
  - Median changes from baseline to Week 48 were -0.04 (Cohort 3) and 0.07 (Cohort 2)

For CD4/CD8 T-cell results, please scan the QR code

Reference values in children without HIV[1]

- 10th and 90th percentiles for children aged ≥ 2 to < 6 years
- Median for children aged ≥ 2 to < 6 years
- 10th and 90th percentiles for children aged ≥ 6 to < 12 years
- Median for children aged ≥ 6 to < 12 years

References: **1.** Shearer WT, et al. J Allergy Clin Immunol 2003;112:973-980. **2.** Lugada ES, et al. Clin Diagn Lab Immunol 2004;11:29-34. **3.** Geletaw T, et al. J Blood Med 2017;8:99-105. **4.** Vishnu P, Aboulafia DM. Br J Haematol 2015;171:695-709. **5.** NCT01854775. https://clinicaltrials.gov/ct2/show/NCT01854775 (accessed April 28, 2023)

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Abbreviations: ART, antiretroviral therapy; CD, cluster of differentiation; E/C/F/TAF, elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide; EVG, elvitegravir; FTC, emtricitabine; NK, natural killer; PK, pharmacokinetics; Q, quartile; QD, once daily; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil.

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