B/F/TAF In Virologically Suppressed Adolescents and Children: Two-year Outcomes in 6 to <18 Year Olds and Six-month Outcomes in Toddlers

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Disclosures

Introduction

- Despite recent innovations in HIV treatment, the limited availability of once-daily, palatable STR formulations for very young children remains problematic
- Bictegravir (BIC; B) is a novel, unboosted INSTI, with a high resistance barrier and low potential for drug-drug interactions
  - BIC has been coformulated with emtricitabine (FTC; F) and tenofovir alafenamide (TAF) into a once-daily STR (B/F/TAF 50/200/25 mg)
  - Can be taken without regard to food
- B/F/TAF 50/200/25 mg is a guideline-preferred treatment option for adults and children weighing ≥25 kg living with HIV-1[1-5]
- Moreover, B/F/TAF has been formulated as a low-dose STR for children aged ≥2 y and weighing 14–<25 kg
  - Low-dose STR strength is B/F/TAF 30/120/15 mg (60% of adult-strength STR)
- We present long term safety, efficacy, and tolerability outcomes in virologically suppressed 6 to <18-year-olds who received B/F/TAF through 96 weeks, and results in younger children aged ≥2 y who received the new formulation, B/F/TAF low-dose tablet through 24 weeks

INSTI, integrase strand transfer inhibitor; STR, single tablet regimen.

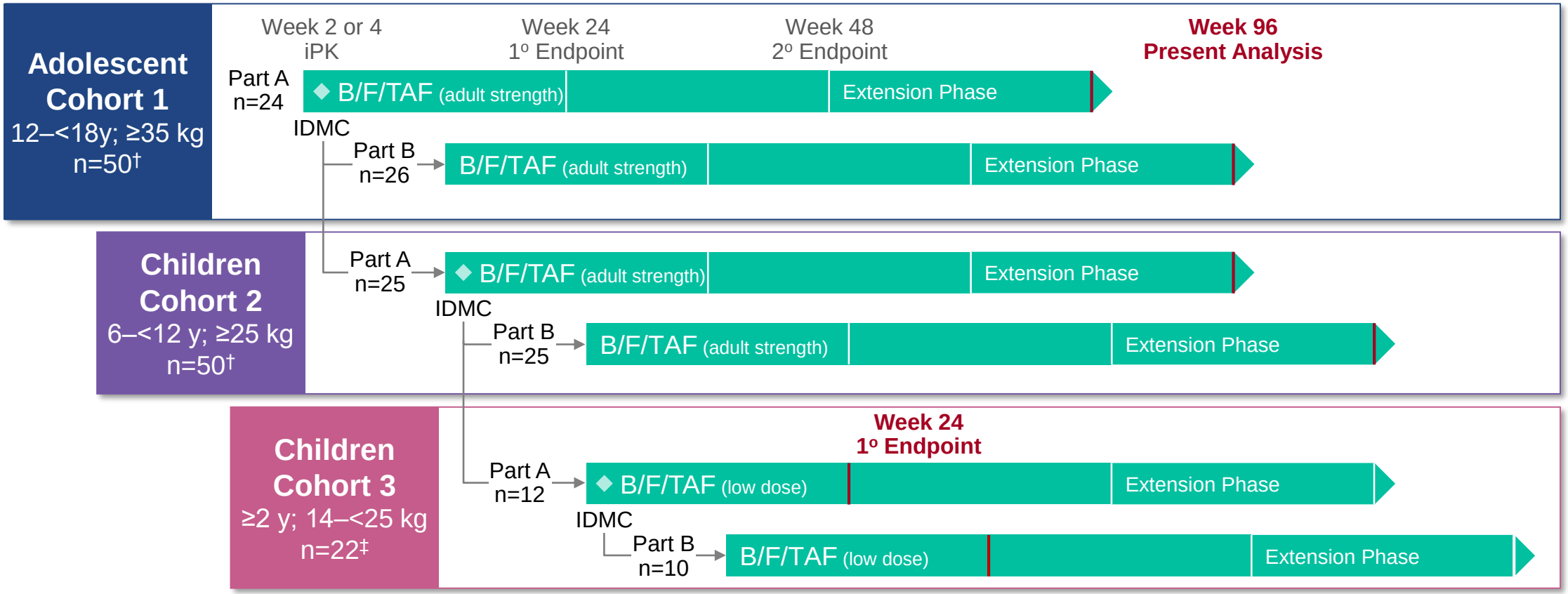
1. AIDSinfo. https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/whats-new-guidelines: 02/21; 2. Biktarvy [package insert]. Foster City, CA: Gilead Sciences, Inc: 02/21; 3. Gallant JE, et al. J Acquir Immune Defic Syndr 2017;75:61-6; 4. Tsiang M, et al. Antimicrob Agents Chemother 2016.60:7086-97; 5. Clinicalinfo.hiv.gov. https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/whats-new-guidelines: 04/21.

Study Design

Eligibility Criteria

- HIV-1 RNA <50 copies/mL for ≥6 mo
- CD4 count ≥200 cells/μL
- eGFR ≥90 mL/min/1.73 m^2 (Schwartz)

- Phase 2/3, open-label, multicenter, multi-cohort, single-arm study (NCT02881320)
  - Part A: iPK was assessed to confirm dose of B/F/TAF
  - Part B: following dose confirmation and IDMC review* of short-term safety from Part A, additional participants were enrolled to complete the cohort and initiate enrollment into the next younger cohort



*Independent data monitoring committee (IDMC) review occurred when 50% of participants reached Week 12 and all completed iPK (intensive PK) visit; †Previously reported;[5,6] ‡6 children switched to adult-strength tablet when they exceeded 25 kg. CD4, cluster of differentiation-4; eGFR, estimated glomerular filtration rate.

Objectives

- Primary: to determine the plasma PK of BIC, and evaluate the safety and tolerability of B/F/TAF through 24 wk of treatment in virologically suppressed adolescents (Cohort 1) and children (Cohorts 2 and 3) living with HIV[1-6]

- Secondary: to evaluate the safety and tolerability of B/F/TAF through 48 wk, and its antiviral activity at 24 and 48 wk, in virologically suppressed adolescents (Cohort 1) and children (Cohorts 2 and 3) living with HIV[1-6]

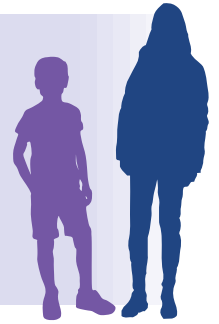
- **Present analyses focus on outcomes from Cohorts 1 and 2 through Week 96 and Cohort 3 through Week 24**

1. Gaur A, et al. CROI 2018; 2. Cotton MF, et al. AIDS 2018; 3. Gaur A, et al. CROI 2019; 4. Rodriguez CA, et al. CROI 2020; 5. Majeed SR, et al. CROI 2020; 6. Liberty A, et al. Intl Workshop on HIV Peds 2020.

Study Drug

- B/F/TAF low-dose tablet 30/120/15 mg
  Mass: 433 mg
  - Evaluated regimen for children ≥2 y and 14–<25 kg

- B/F/TAF adult-strength tablet 50/200/25 mg
  Mass: 721 mg
  - *Preferred* ARV regimen for children ≥6 y and ≥25 kg[1]



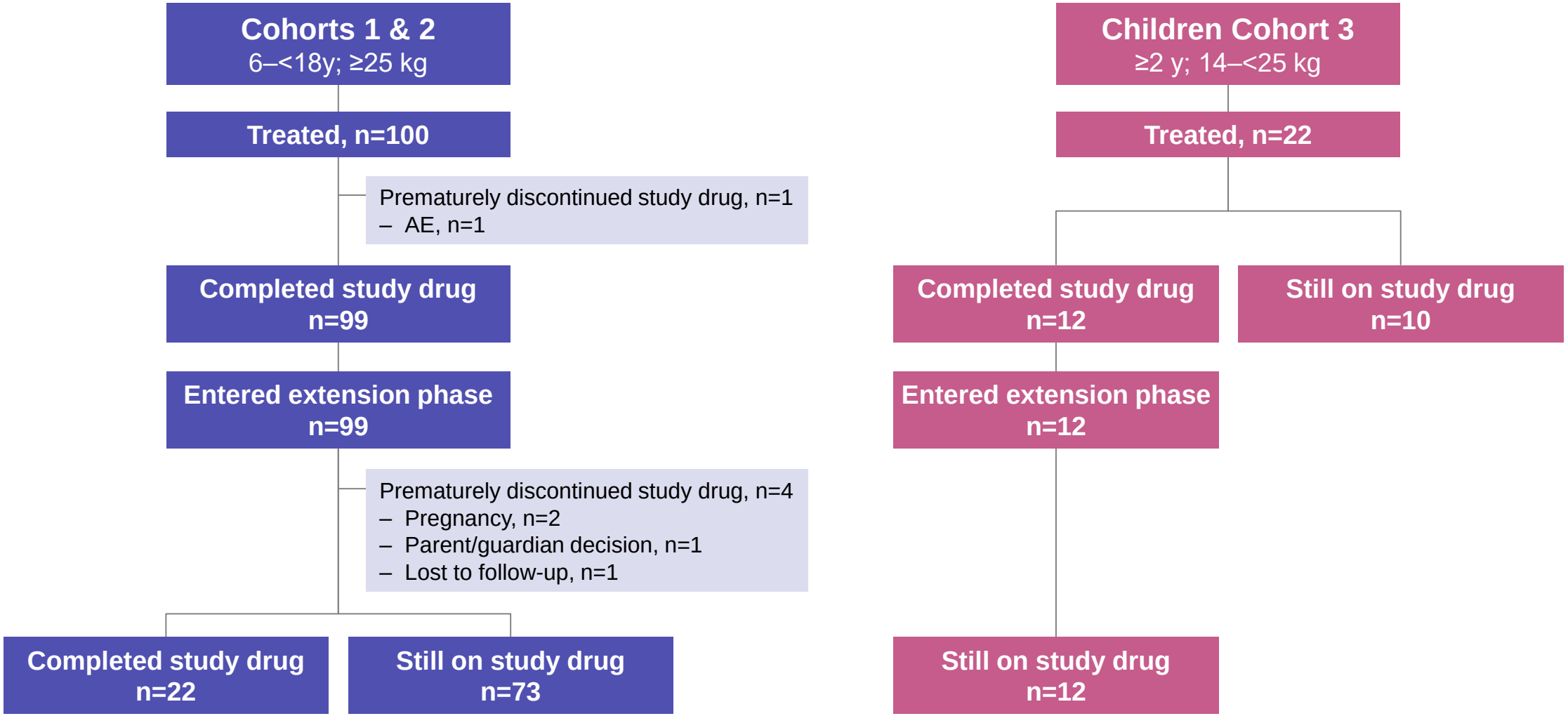
1. Clinicalinfo.hiv.gov. https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/whats-new-guidelines: 04/21

Study Assessments

- **PK**: intensive PK samples collected to confirm steady-state exposure of BIC, FTC and TAF
- **Safety**: AEs and clinical laboratory abnormalities
- **Efficacy**: HIV-1 RNA and CD4 cell count
- **Palatability and Acceptability**: questionnaires and facial scale
- **Adherence**: assessed by pill count at each visit

AE, adverse event; PK, pharmacokinetics.

Disposition: Adolescents and Children

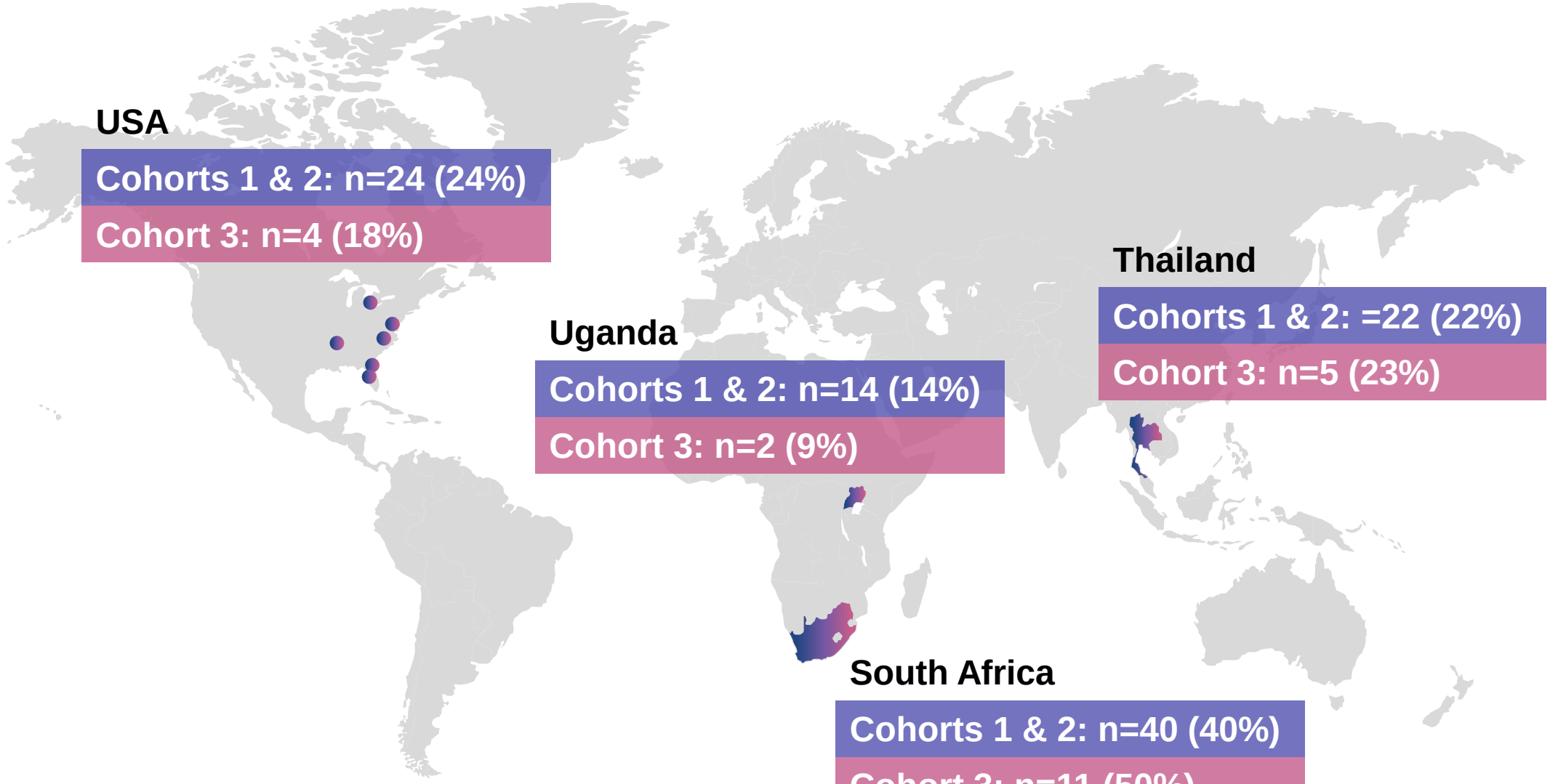


Baseline Characteristics

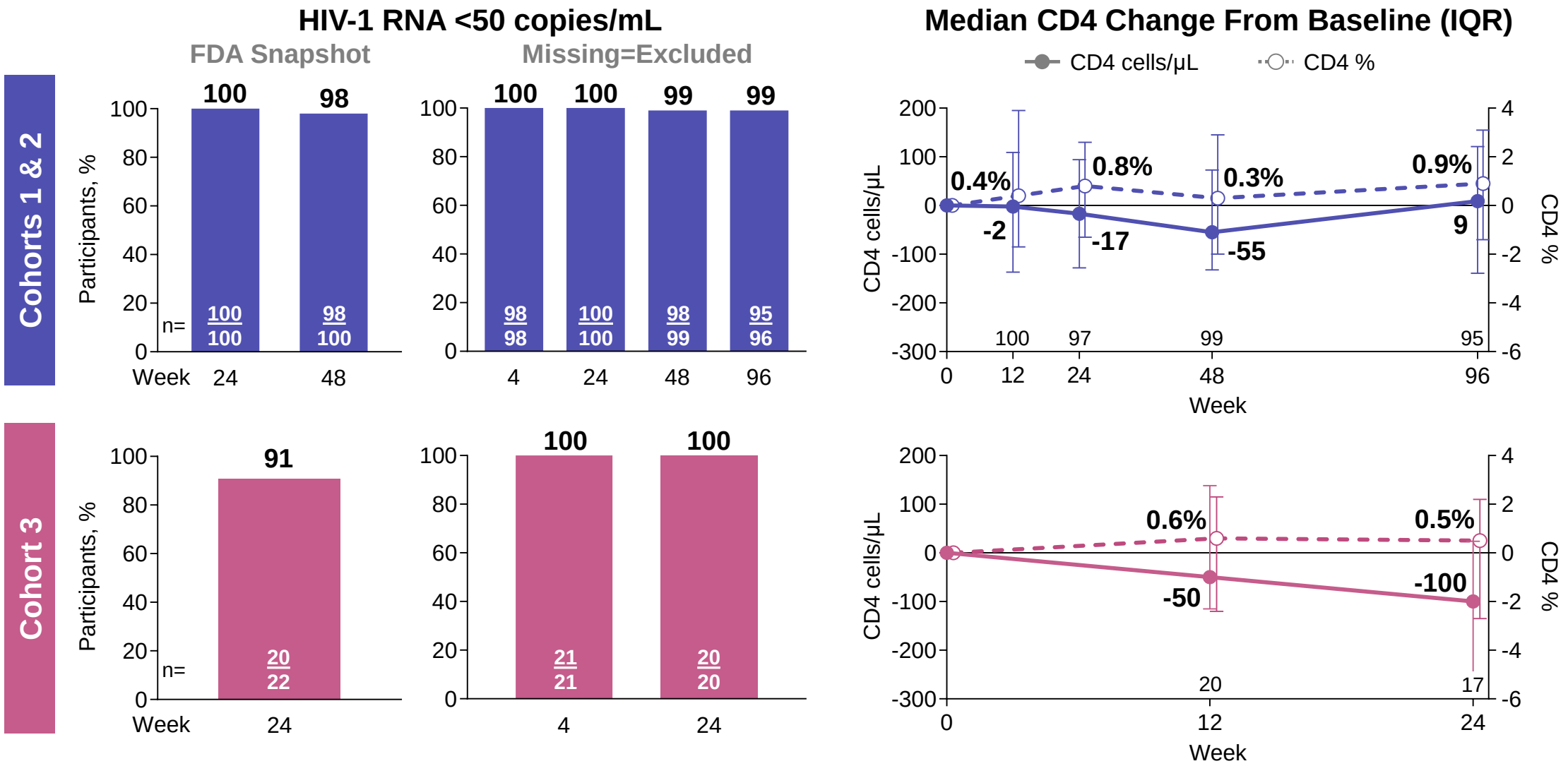
	Cohort 1 12–<18y; ≥35 kg n=50	Cohort 2 6–<12 y; ≥25 kg n=50	Cohort 3 ≥2 y; 14–<25 kg n=22
Median age, y (range)	15 (12 – 17)	10 (6 – 11)	6 (3 – 9)
Median weight, kg (Q1, Q3)	44.8 (40.0, 56.1)	29.0 (26.9, 32.5)	18.7 (15.2, 21.7)
Female at birth, n (%)	32 (64)	27 (54)	11 (50)
Race, n (%)*			
Asian	13 (27)	11 (22)	5 (23)
Black	32 (65)	36 (72)	16 (73)
Native Hawaiian or Pacific Islander	1 (2)	0	0
White	1 (2)	2 (4)	0
Other	2 (4)	1 (2)	1 (5)
HIV-1 RNA <50 copies/mL, n (%)	50 (100)	50 (100)	22 (100)
Median CD4 cells/μL (Q1, Q3)	750 (586, 926)	898 (707, 1121)	962 (748, 1419)
Median CD4 % (Q1, Q3)	32.9 (28.5, 38.2)	36.5 (31.9, 41.1)	32.0 (29.3, 37.2)
Median years since HIV diagnosis (Q1, Q3)	12 (10, 14)	10 (7, 11)	4 (3, 5)
Vertical transmission, n (%)	45 (90)	48 (96)	22 (100)
Asymptomatic HIV disease status, n (%)	46 (92)	47 (94)	20 (91)
Median $eGFR_{Schwartz}$, mL/min/1.73m^2 (Q1, Q3)	145.0 (134.0, 170.0)	153.5 (144.0, 173.0)	160.5 (145.0, 168.0)

*1 participant in Cohort 1 did not report race and ethnicity and was excluded from the race categorization and percentage calculation.

Enrollment by Country



Efficacy: Virologic Outcomes



- No participant developed treatment-emergent resistance

Overall Safety: Cohorts 1, 2 and 3

n (%)	Cohorts 1 & 2 n=100	Cohort 3 n=22
Median exposure to study drug, wk (IQR)	151.4 (125.6, 153.5)	54.9 (29.3, 66.4)
Any AE, n (%)	86 (86)	17 (77)
Any grade AE in ≥10% either group, n (%)		
Upper respiratory tract infection	30 (30)	5 (23)
Cough	15 (15)	3 (14)
Nasopharyngitis	11 (11)	3 (14)
Diarrhea	11 (11)	2 (9)
Headache	11 (11)	2 (9)
Vomiting	8 (8)	3 (14)
AE related to study drug	13 (13)	3 (14)
Grade 3–4 AE	5 (5)	0
Serious AE	5 (5)	0
AE leading to study drug discontinuation	1 (1)	0
Death	0	0

- Study drug-related AEs reported in >1 participant included abdominal discomfort (n=3) and transient neutropenia (n=2)
- One participant discontinued around Week 20 due to an AE (grade 2 insomnia and anxiety, Cohort 2)

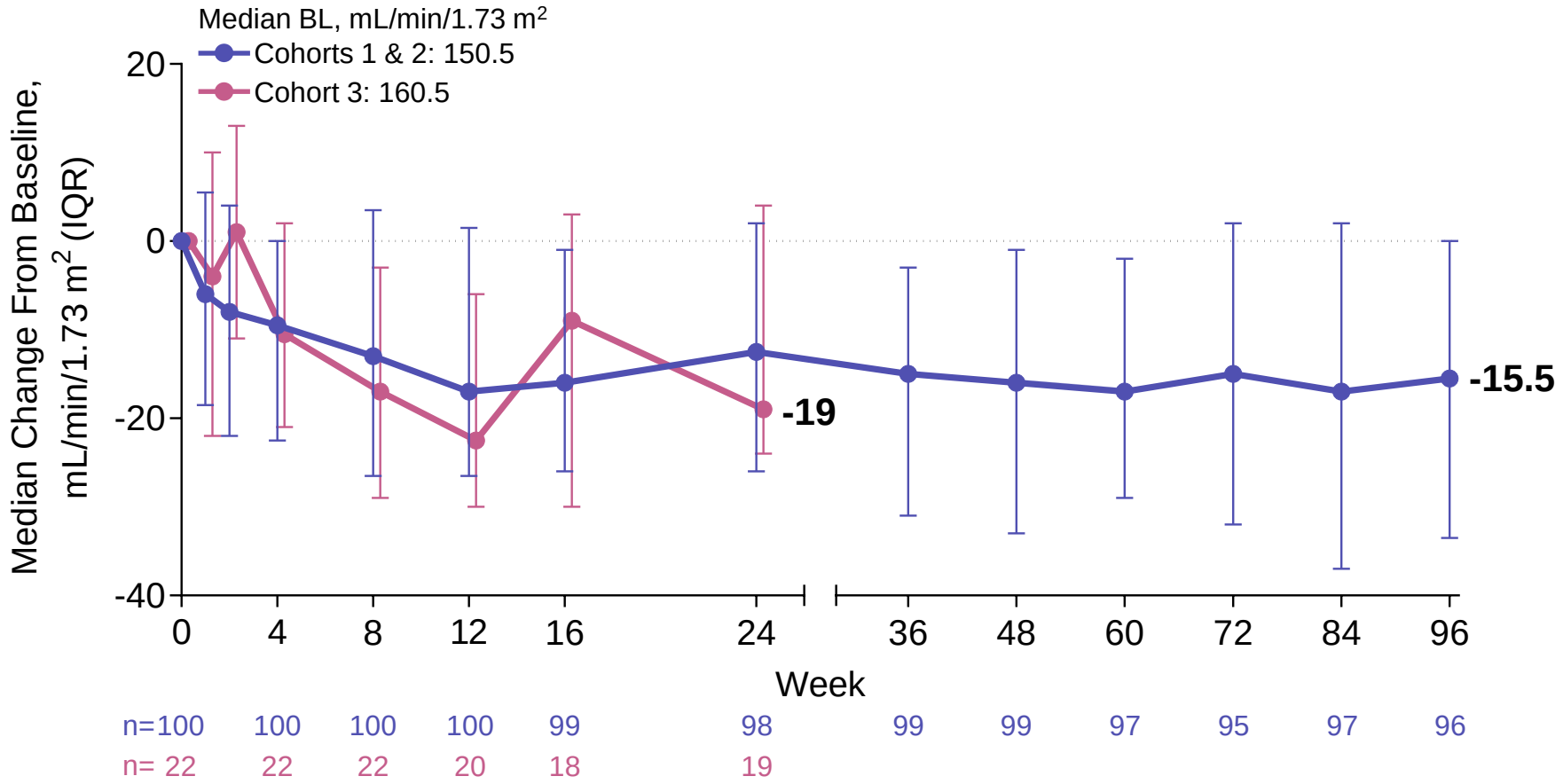
Treatment Emergent Grade 3 or 4 Laboratory Abnormalities

n (%)	Cohorts 1 & 2 n=100	Cohort 3 n=22
Any treatment-emergent Grade 3 or 4 laboratory abnormalities	30 (30)	4 (18)
Treatment-emergent Grade 3 or 4 laboratory abnormalities		
Neutrophils decreased	8 (8)	3 (14)
Alkaline phosphatase increased	0	1 (5)
ALT increased	1 (1)	0
Amylase increased	3 (3)	0
AST increased	1 (1)	0
Bicarbonate decreased	1 (1)	0
Creatinine increased	0	1 (5)
Magnesium (hypomagnesemia)	1 (1)	0
Serum potassium (hyperkalemia)	2 (2)	0
Urine RBC (hematuria, quantitative or dipstick)	16 (16)	0

- Cohorts 1 & 2: Most frequent Grade 3 or 4 laboratory abnormality was hematuria (n=16 [16%]), most related to menses

ALT, alanine aminotransferase; AST, aspartate aminotransferase; RBC, red blood cell.

Estimated Glomerular Filtration Rate (Schwarz)

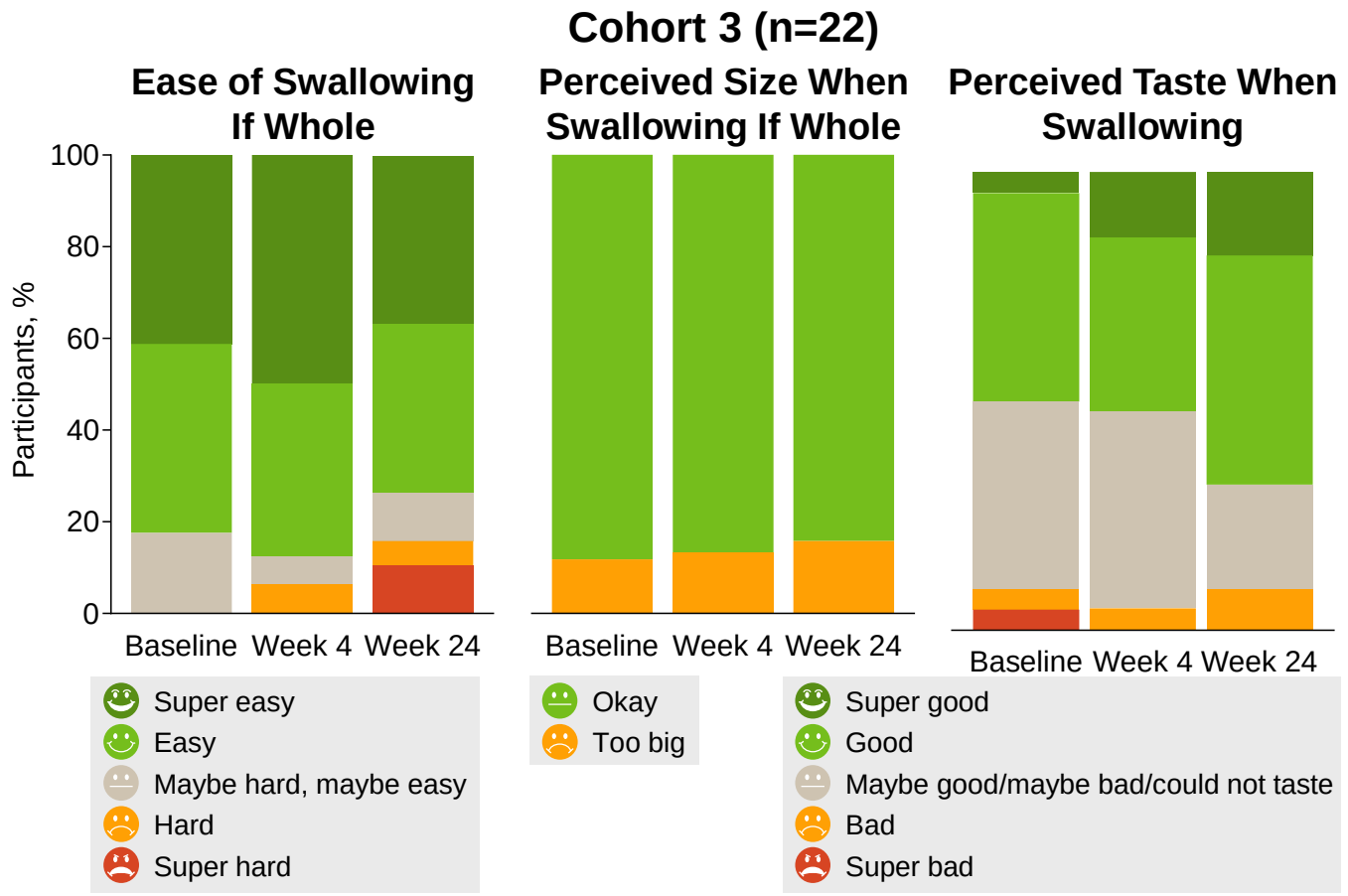


- Median changes in eGFR ranged from +1 to -23 mL/min/1.73m^2 between Weeks 1 and 96
- Initial decline and stabilization of eGFR in children weighing 14–<25 kg are consistent with the known renal creatinine transporter effect of BIC[1,2] and not considered clinically significant

1. Rodriguez CA, et al. CROI 2020; 2. Majeed SR, et al. CROI 2020.

Tablet Acceptability and Adherence

- Acceptability and palatability assessments: facial scale and age-appropriate labels to rate ease or difficulty in swallowing tablet
  - Acceptability of tablet shape and size, and assessment of tablet taste
- **Cohorts 1 & 2:** all participants reported B/F/TAF size/shape acceptable and taste as palatable at Day 1 and Week 4
- Median adherence by pill count to B/F/TAF
  - In Cohorts 1 & 2, 99% up to Weeks 24 and 48, and 98% up to Week 96
  - In Cohort 3, 99% up to Week 24



Conclusions

- In virologically suppressed children and adolescents (aged 6 to <18 y; weight ≥25 kg, adult-strength B/F/TAF) through 96 weeks and children (aged ≥2 y; weight 14–<25 kg, low-dose B/F/TAF) through 24 weeks of follow up:
  - B/F/TAF maintained virologic suppression with no treatment-emergent resistance
  - Both adult-strength and low-dose formulations were well tolerated
  - Acceptability and palatability of the low-dose STR was high, even down to age 3 y
- Efficacy and safety are consistent with results from Phase 3 trials of B/F/TAF in adults, which showed high proportions with viral suppression, no resistance, and good tolerability
- Evaluation of an age-appropriate B/F/TAF formulation in infants and children <2 y is planned

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