A Daily Single-Tablet Regimen of Bictegravir/Emtricitabine/Tenofovir Alafenamide in Virologically Suppressed Adults Living With HIV and End-stage Renal Disease on Chronic Hemodialysis



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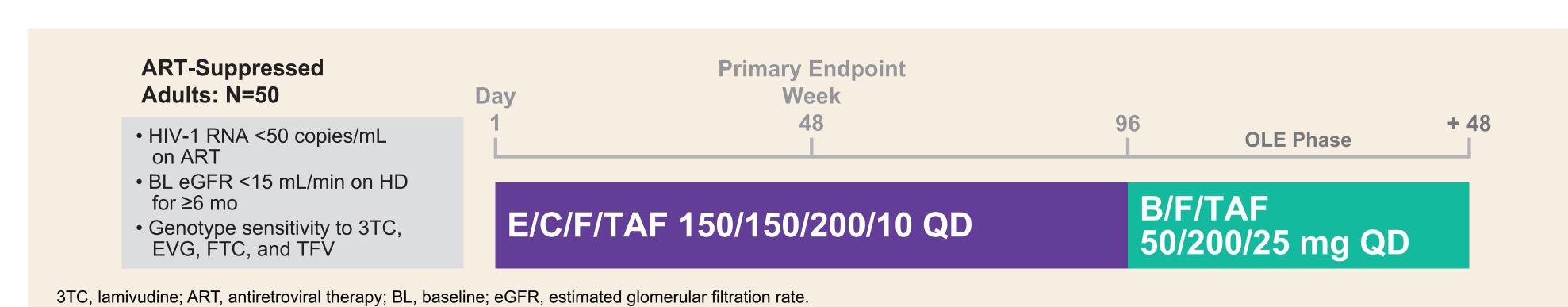
Introduction

- Treatment for people living with HIV (PLWH) and end-stage renal disease (ESRD) on hemodialysis (HD) has previously required complex dose-adjusted regimens
- We previously evaluated elvitegravir (EVG)/cobicistat/emtricitabine (FTC)/tenofovir (TFV) alafenamide (TAF; E/C/F/TAF) daily, and established this treatment as effective and safe, showing that daily TAF resulted in lower plasma TFV exposure than a historical comparison of once-weekly TFV disoproxil fumarate in patients with ESRD on HD^{1,2}
- ◆ The single-tablet regimen (STR) bictegravir (BIC)/FTC/TAF (B/F/TAF) is a US DHHS, EACS, and IAS-USA guidelines-recommended regimen,³⁻⁵ with demonstrated safety and efficacy, a high barrier to resistance, and limited potential drug-drug interactions
- Based on B/F/TAF Phase 3 data and FDA approval, the protocol was amended to allow eligible US participants to enroll in an open-label extension (OLE) with B/F/TAF

Objectives

◆ To assess the safety and tolerability of the B/F/TAF STR in PLWH with ESRD on chronic HD at Week 48

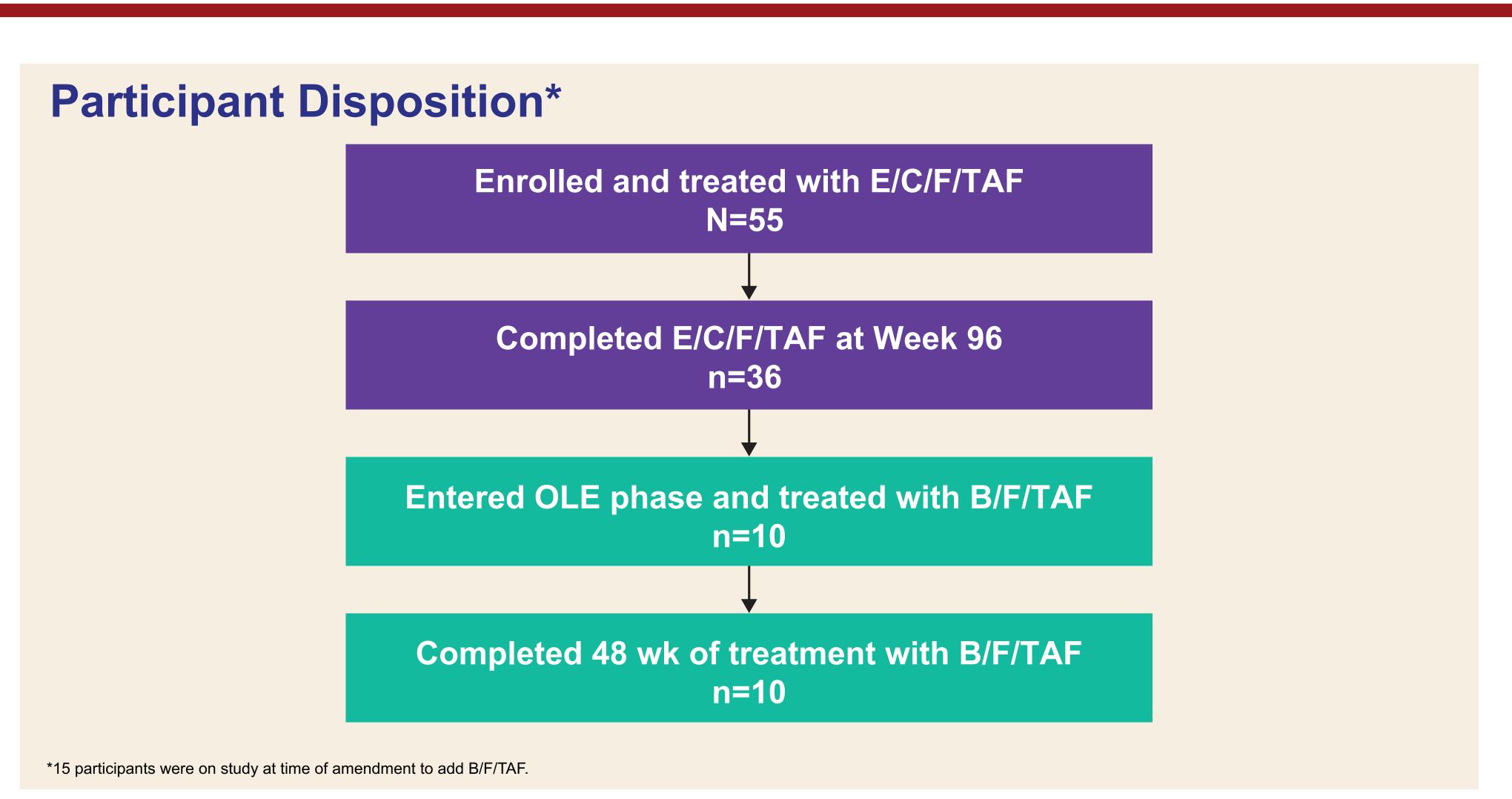
Methods



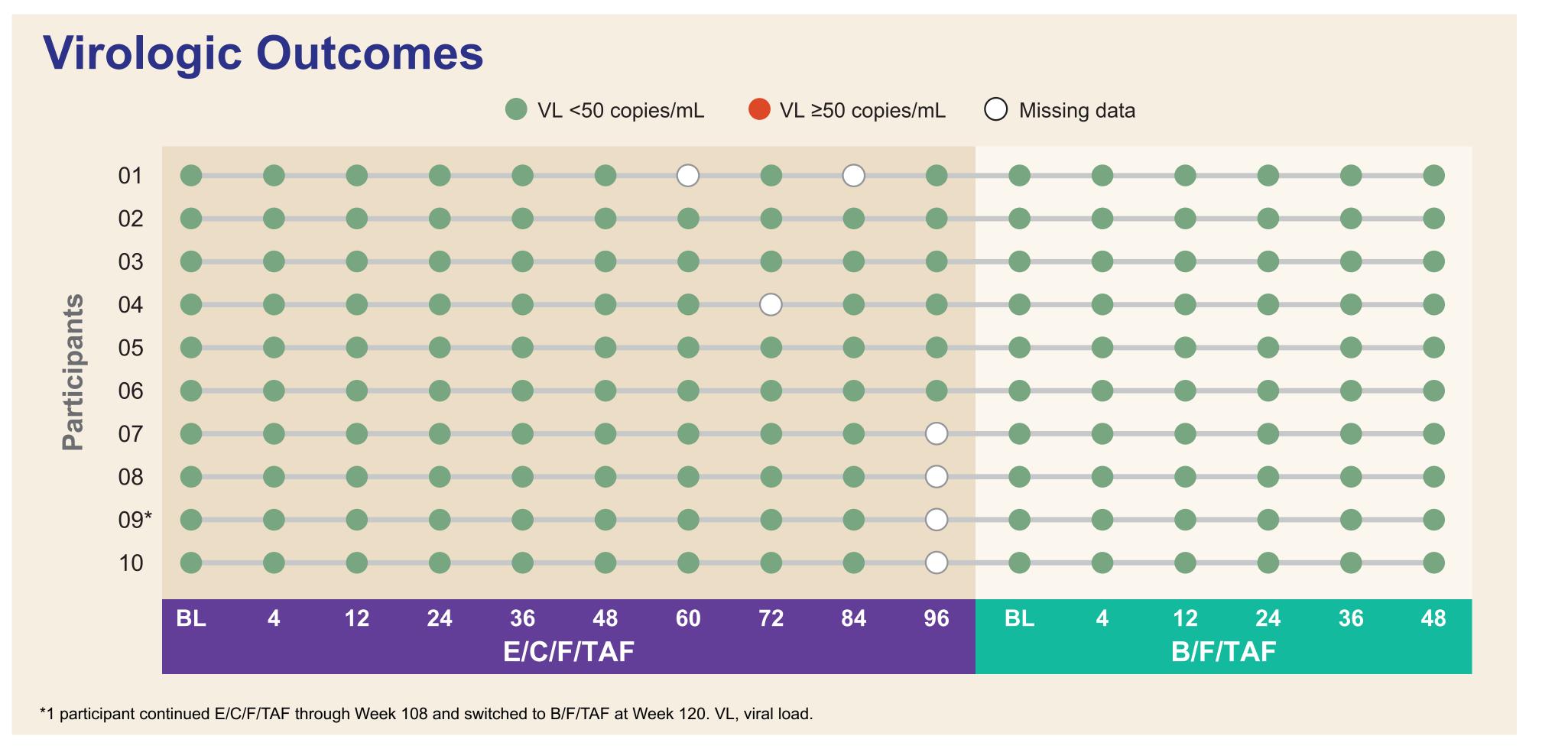
- Phase 3B, open-label, multicenter, single-arm study in North America and Europe (GS-US-292-1825 [NCT02600819])
- Protocol amended in 2018 for US participants after B/F/TAF regulatory approval by FDA
- Participants who remained in study follow-up switched to B/F/TAF in the OLE phase
- Assessments during B/F/TAF OLE:
- Safety: adverse events (AEs) and laboratory abnormalities
- Efficacy: proportion of participants with virologic suppression (HIV RNA <50 copies/mL) by missing = excluded (M=E)
- Pharmacokinetics (PK): sampling at Weeks 4, 24, and 48

Results

| aseline Characteristics | | B/F/TAF: n=10 | |
|---|------------------------|------------------|--|
| Median age at B/F/TAF start, y (range) | | 55 (34–63) | |
| Sex at birth, n (%) | Male | 8 (80) | |
| | Female | 2 (20) | |
| Race, n (%) | Black | 9 (90) | |
| | White | 1 (10) | |
| IV-1 RNA <50 copies/mL | 10 (100) | | |
| ledian CD4 cells/µL at B/ | 563 (451, 705) | | |
| Mode of infection, n (%)* | Heterosexual sex | 6 (60) | |
| | Homosexual sex | 3 (30) | |
| | Injection drug use | 1 (10) | |
| | Unknown | 1 (10) | |
| epatitis C virus antibody | 5 (50) | | |
| Median eGFR _{CG} at B/F/TAF start, mL/min (IQR) [†] | | 11.6 (7.8, 14.6) | |
| Median years on HD (range) | | 4 (2–16) | |
| Medical history, n (%) | Diabetes | 4 (40) | |
| | Hypertension | 10 (100) | |
| | Cardiovascular disease | 6 (60) | |
| | Hyperlipidemia | 3 (30) | |

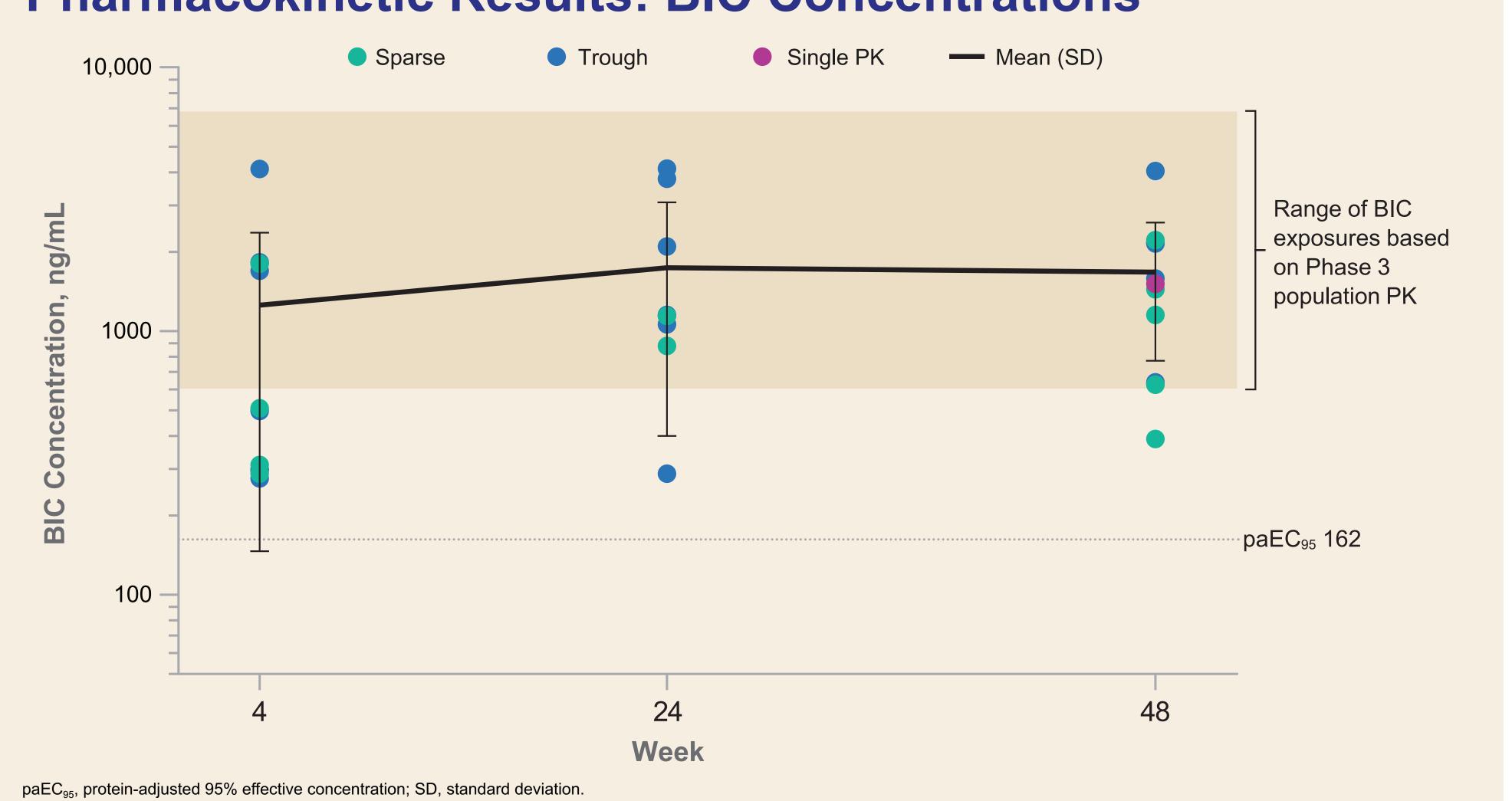


◆ Median duration of exposure to B/F/TAF: 48 wk (range 47–52)



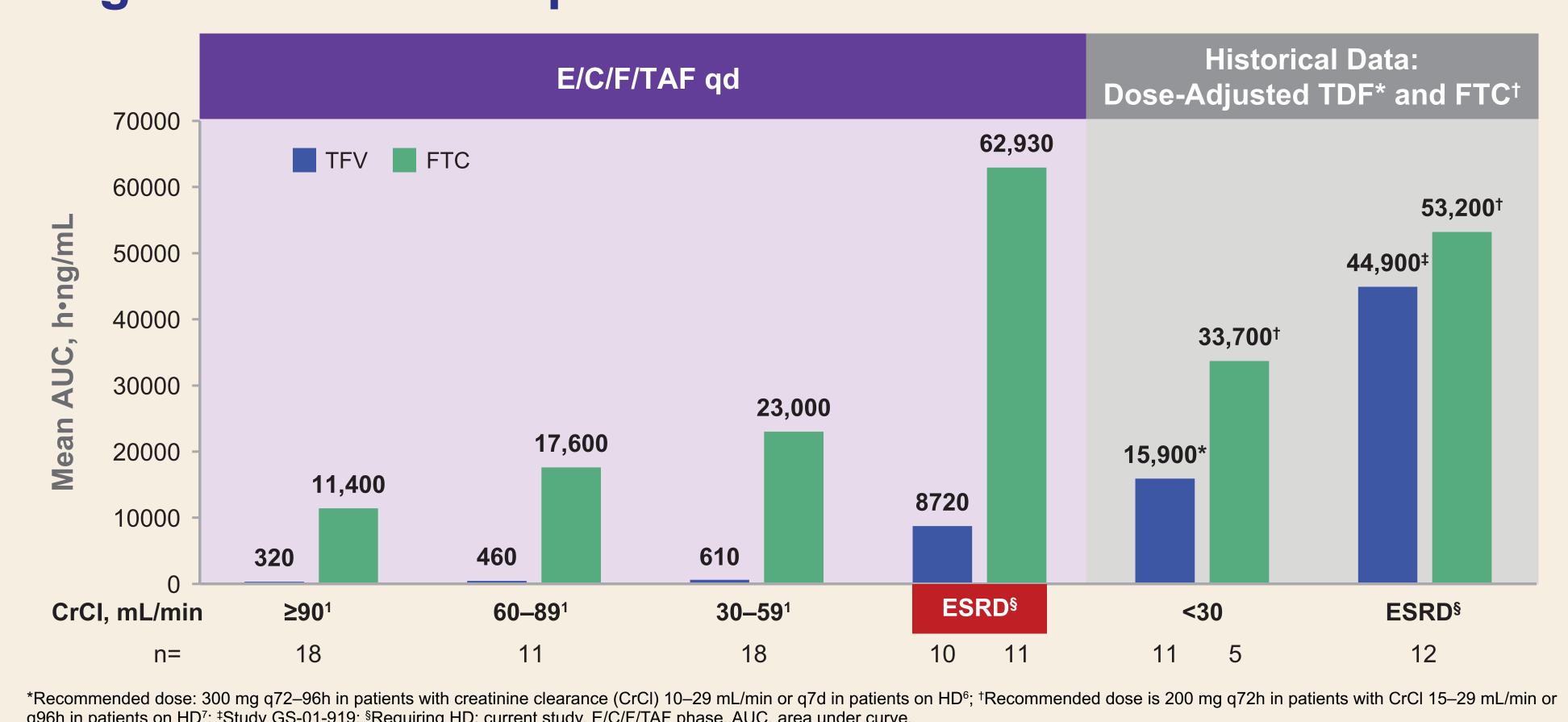
- ◆ At 48 wk after switching to B/F/TAF, all 10 participants (100%) maintained virologic suppression (HIV RNA <50 copies/mL) by M=E
- For the 10 participants who switched to B/F/TAF, median (IQR) CD4 count at BL was 563 (451, 705) cells/μL and median change from BL at Week 48 (n=9) was -121 (IQR -144, -21) cells/μL
- No participants met the criteria for resistance testing

Pharmacokinetic Results: BIC Concentrations



- ◆ In participants with available data, mean BIC concentrations were lower vs PLWH not on HD
- BIC trough concentrations remained 4- to 7-fold higher than the BIC established paEC₉₅ of 162 ng/mL against wild-type virus from Phase 3 study results

TFV and FTC Exposures Among Adults With Various Degrees of Renal Impairment¹



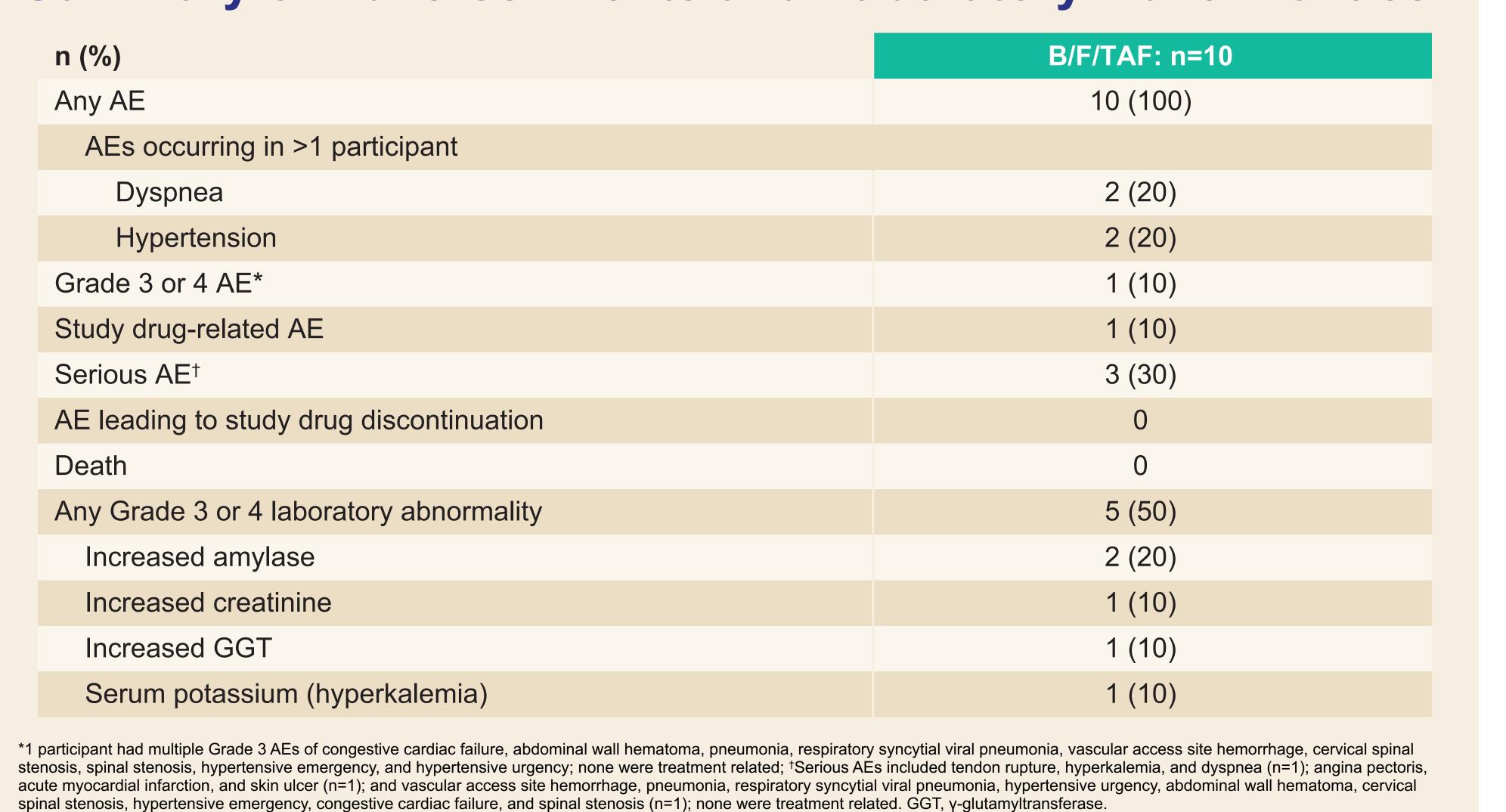
- ◆ FTC and TFV exposures were higher in individuals on HD vs historical data from E/C/F/TAF in HIV-1—infected adults with normal renal function or mild—moderate renal impairment
- TFV exposures were substantially lower than historical data with TDF dosed once weekly in HD
- ◆ FTC exposures were similar to historical data with FTC in HD

Pharmacokinetic Results: TAF and FTC¹

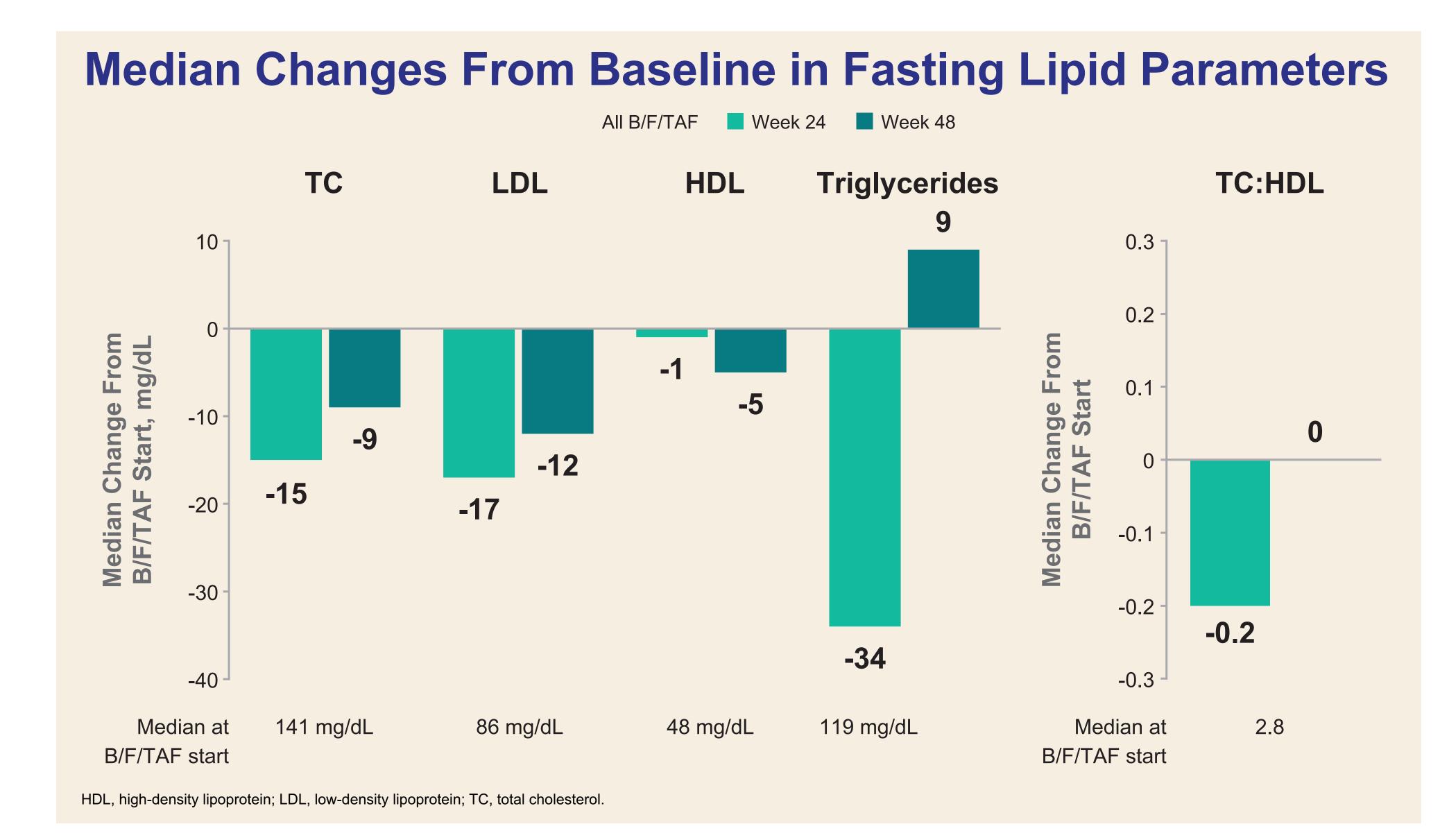
| | | E/C/F/TAF | | | | |
|---------------------|---------------------|-----------|-------------|-----|-----------------------|--|
| Mean, h·ng/mL (%CV) | | n | ESRD | n | Normal Renal Function | |
| FTC | AUC _{tau} | 11 | 62,900 (48) | 18* | 11,400 (12) | |
| TAF | AUC _{last} | 12 | 232 (53) | 18* | 230 (47) | |
| TFV | AUC _{tau} | 10 | 8720 (39) | 18* | 320 (15) | |

- Exposures of TAF, hepatically metabolized, were consistent with the ranges of historical data in PLWH with normal renal function⁸
- ◆ As expected, exposures of the renally eliminated metabolite TFV were higher than with TAF in normal renal function
- Exposures of FTC, also renally eliminated, were higher than in individuals with normal renal function, but safety profile was similar

Summary of Adverse Events and Laboratory Abnormalities

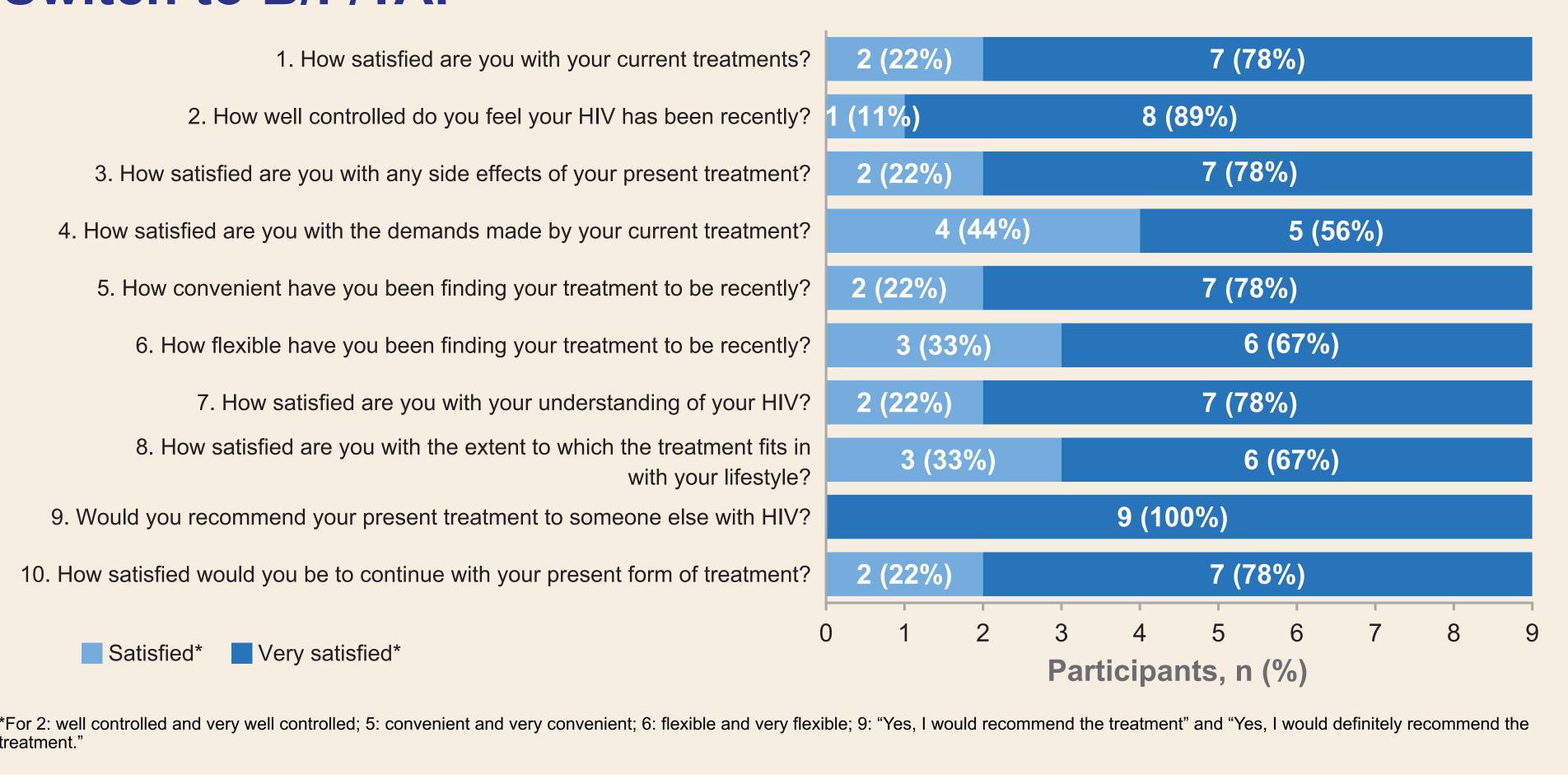


- Most AEs were Grade 1 or 2 in severity
- 1 participant had study-drug related AEs of Grade 2 nausea and Grade 1
- No Grade ≥3 or serious AEs were considered related to study drug



- ◆ There were no clinically relevant changes from BL in median fasting lipid parameters at Weeks 24 and 48 after switching to B/F/TAF
- No participants initiated lipid-modifying agents after switch

HIV Treatment Satisfaction and Adherence at Week 48 After Switch to B/F/TAF



 Median adherence through Week 48 was 89% (IQR 84, 98) as measured by pill count

Conclusions

- ◆ In this 1st evaluation of the once-daily B/F/TAF STR in PLWH with ESRD on HD, all participants maintained virologic suppression
- ◆ B/F/TAF had a favorable safety and tolerability profile over 48 wk, with no discontinuations
- In participants with evaluable data, mean BIC concentrations were lower compared with PLWH not on HD
- ◆ BIC trough concentrations remained 4- to 7-fold higher than the BIC established paEC₉₅ against wild-type virus from Phase 3 study results
- Simplification to the B/F/TAF STR offers an effective, safe, and convenient once-daily option for PLWH on HD, who often have complicated HIV dosing schedules, multiple comorbidities, and a high pill burden

References: 1. Eron JJ Jr, et al. CROI 2018, poster P-N02; 2. Eron JJ Jr, et al. Lancet HIV 2018;S2352-3018(18)30296-0; 3. Clinical Info HIV.gov. Guidelines for the Use of Antiretroviral Agents in Adults and Adolest Living with HIV; 7/10/19; 4. EACS Guidelines Version 10.1 October 2020; 5. Saag MS, et al. JAMA 2018;320:379-96; 6. Viread [package insert]. Foster City, CA: Gilead Sciences, Inc., 4/17; 8. Genvoya [package insert]. Foster City, CA: Gilead Sciences, Inc., 4/17; 8. Genvoya [package insert]. Foster City, CA: Gilead Sciences, Inc., 4/17; 8. Genvoya [package insert]. Foster City, CA: Gilead Sciences, Inc., 4/17; 8. Genvoya [package insert]. Foster City, CA: Gilead Sciences, Inc., 12/18. Acknowledgments: We extend our thanks to the participants, their families, and all study