5-Year Outcomes of Bictegravir/Emtricitabine/Tenofovir Alafenamide as Initial Treatment of HIV-1 in Adults With High Baseline HIV-1 RNA and/or Low CD4 Count in Two Phase 3 Randomized Clinical Trials



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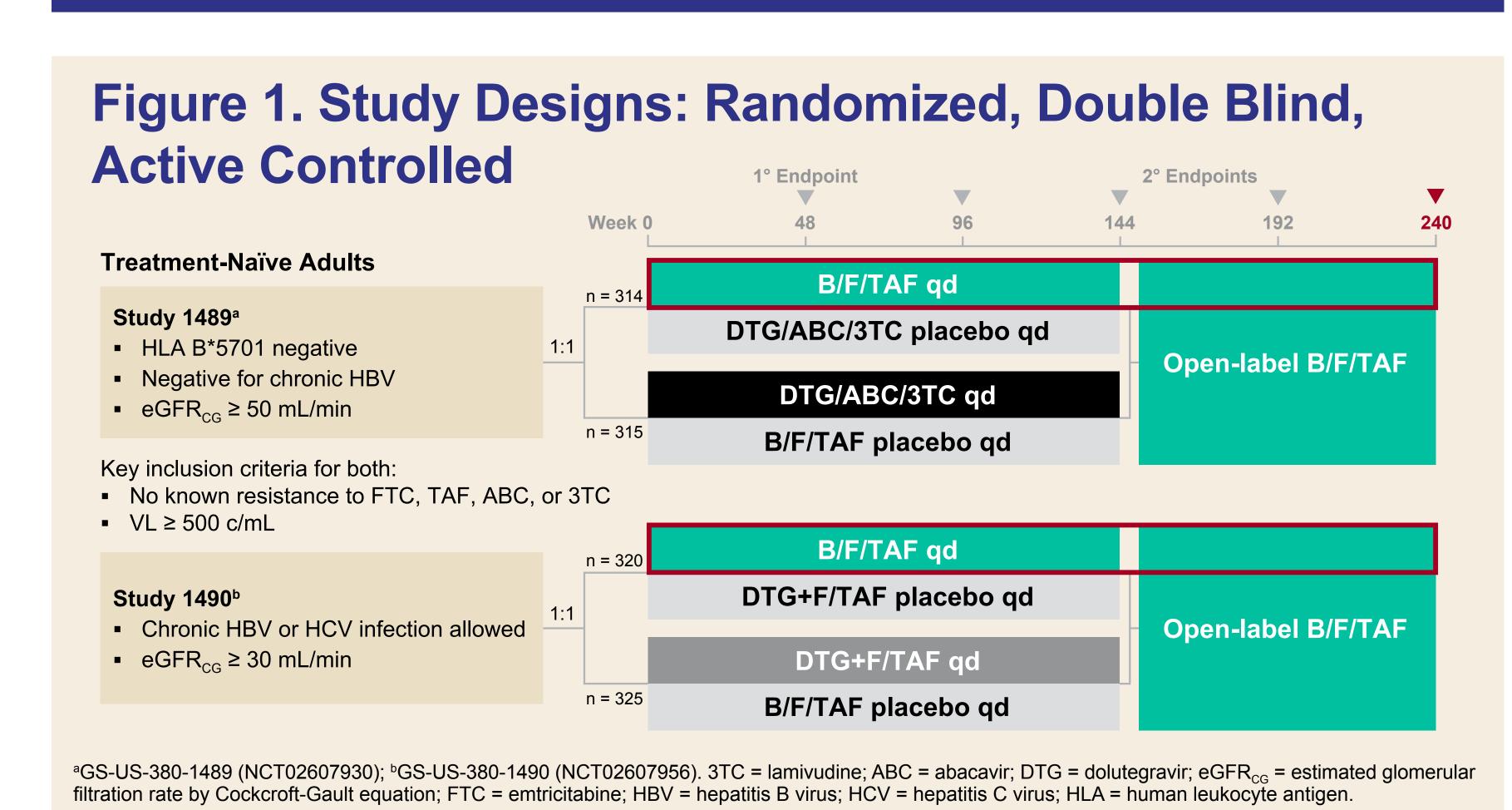
Introduction

- ◆ Early initiation of antiretroviral therapy is associated with improvements in morbidity and mortality, and better immunologic recovery in people with HIV (PWH)¹-³
- ◆ PWH who have advanced disease, ie, those with high HIV-1 RNA viral load (VL) and/or low CD4 count at baseline (BL), are more challenging to manage in the short and long term⁴-7
- ◆ Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is a guidelinerecommended first-line regimen for most PWH; additionally, it is recommended for rapid initiation due to its high barrier to resistance, favorable drug-drug interaction profile, and once-daily dosing without food restrictions⁸⁻¹²

Objective

- ◆ To assess pooled outcomes from Studies 1489 and 1490 through Week 240 in participants initially randomized to B/F/TAF stratified by:
- BL VL < 100,000, 100,000-400,000, and > 400,000 c/mL
- BL CD4 < or ≥ 200 cells/µL
- BL VL ≥ 100,000 c/mL and CD4 < 200 cells/μL

Methods



Results

Figure 2. Participants Randomized to B/F/TAF: Disposition Through Week 240

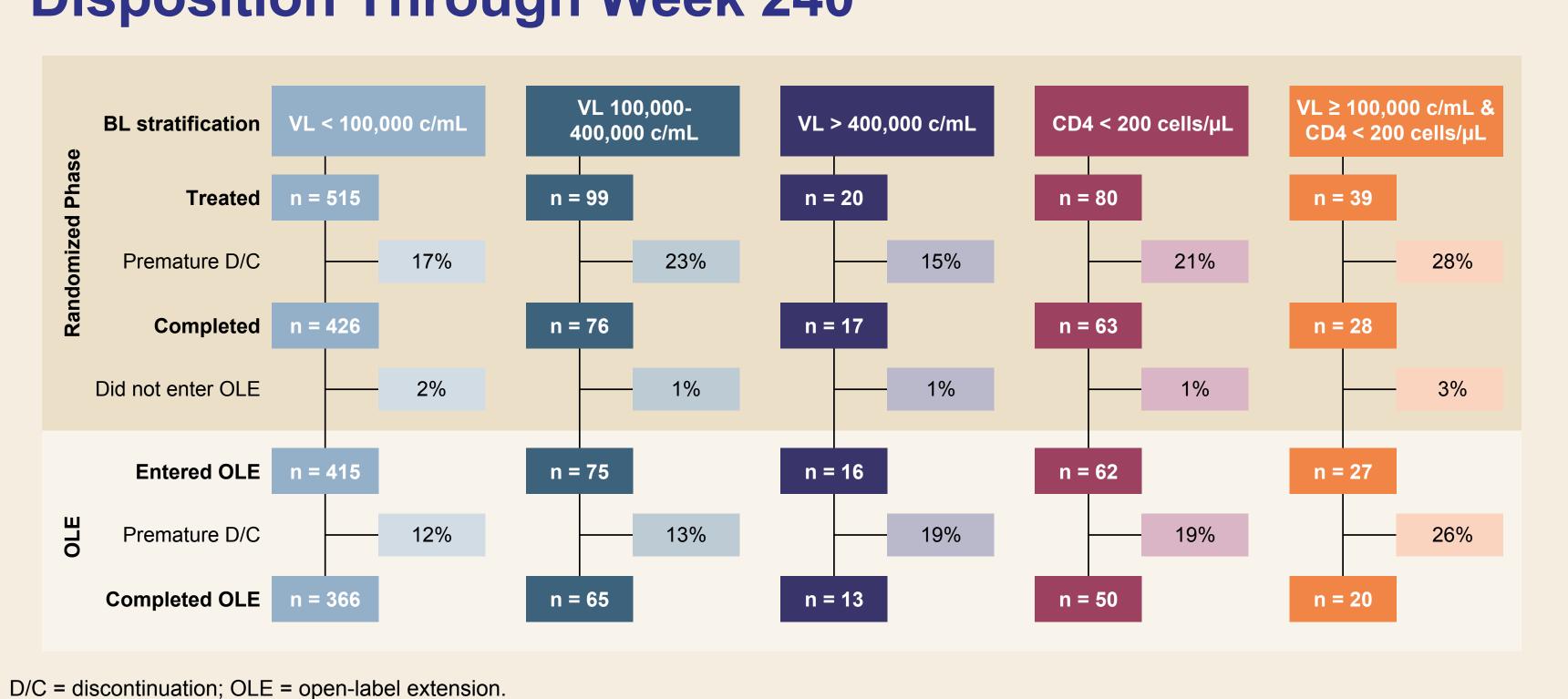


Table 1. Baseline Characteristics

	BL Stratification					
	VL < 100,000 c/mL n = 515	VL 100,000- 400,000 c/mL n = 99	VL > 400,000 c/mL n = 20	CD4 ≥ 200 Cells/µL n = 554	CD4 < 200 Cells/µL n = 80	VL ≥ 100,000 c/mL & CD4 < 200 Cells/µL n = 39
Median age, y (range)	32 (18-71)	33 (18-71)	35 (23-68)	31 (18-71)	36 (22-64)	36 (22-64)
Female at birth, n (%)	64 (12)	5 (5)	0	59 (11)	10 (13)	1 (3)
Race/ethnicity, n (%)						
Black or African descent	169 (33)	35 (36)	7 (35)	174 (32)	37 (47)	18 (47)
Hispanic/Latinx	137 (27)	17 (17)	1 (5)	139 (25)	16 (20)	4 (10)
Median body weight, kg (Q1, Q3)	77.5 (68.2, 89.2)	74.8 (66.7, 84.8)	73.9 (64.9, 83.3)	77.2 (68.2, 88.0)	71.5 (64.5, 84.7)	71.9 (63.5, 85.3)
Median BMI, kg/m² (Q1, Q3)	25.3 (22.4, 29.0)	24.0 (21.7, 26.9)	23.8 (22.5, 29.0)	25.2 (22.4, 28.8)	24.1 (21.2, 26.5)	24.0 (21.2, 25.9)
Asymptomatic HIV infection, n (%)	481 (93)	79 (80)	12 (60)	532 (96)	40 (50)	16 (41)
Median eGFR _{CG} , mL/min (Q1, Q3)	122 (105, 144)	122 (102, 144)	124 (100, 135)	123 (105, 144)	118 (95, 136)	122 (95, 142)
I = body mass index; Q = quartile.						

Figure 3. Virologic Outcomes by Subgroup: VL < 50 c/mL

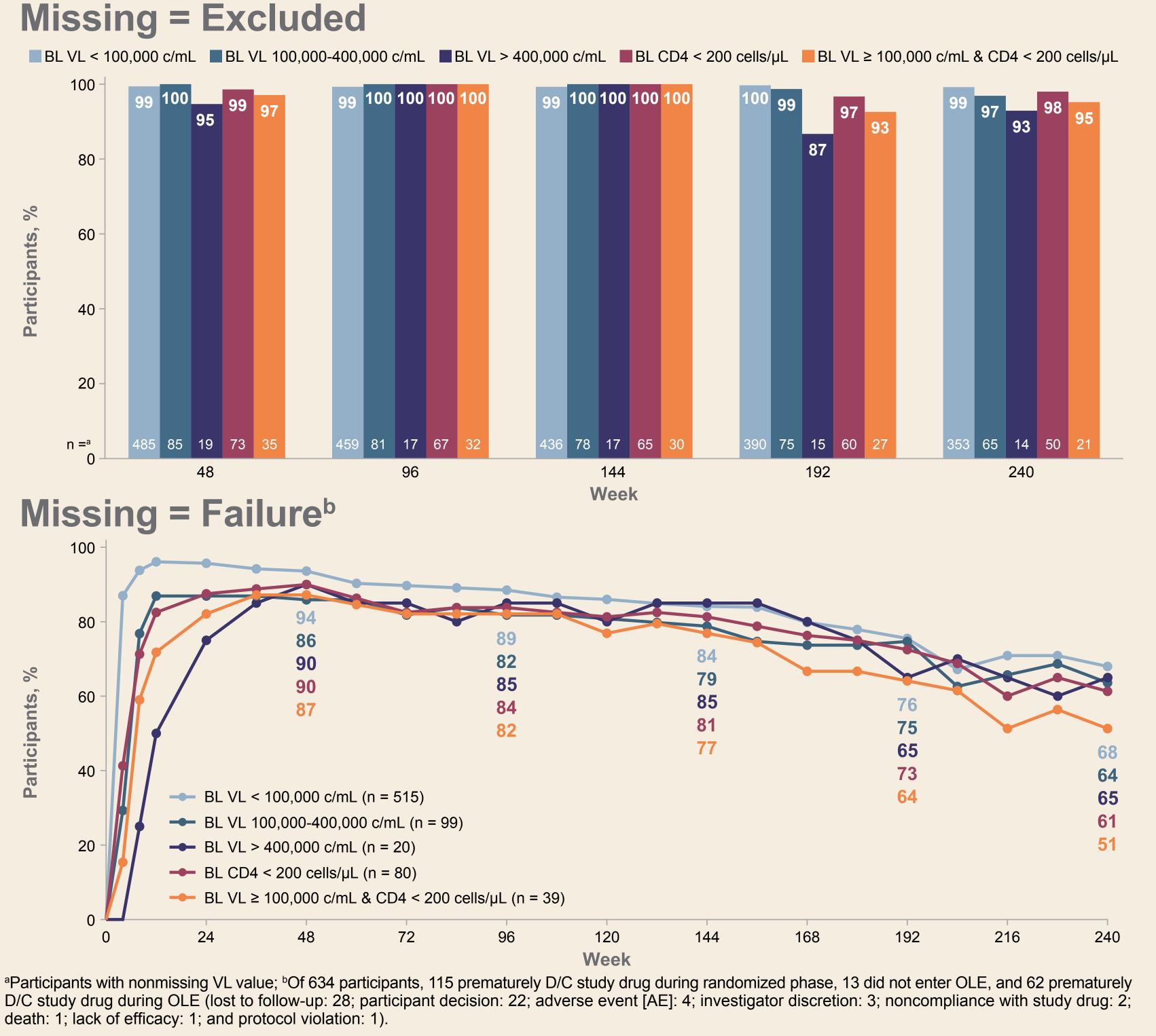


Figure 4. Virologic Outcomes Over Time in Participants With BL VL > 400,000 c/mL

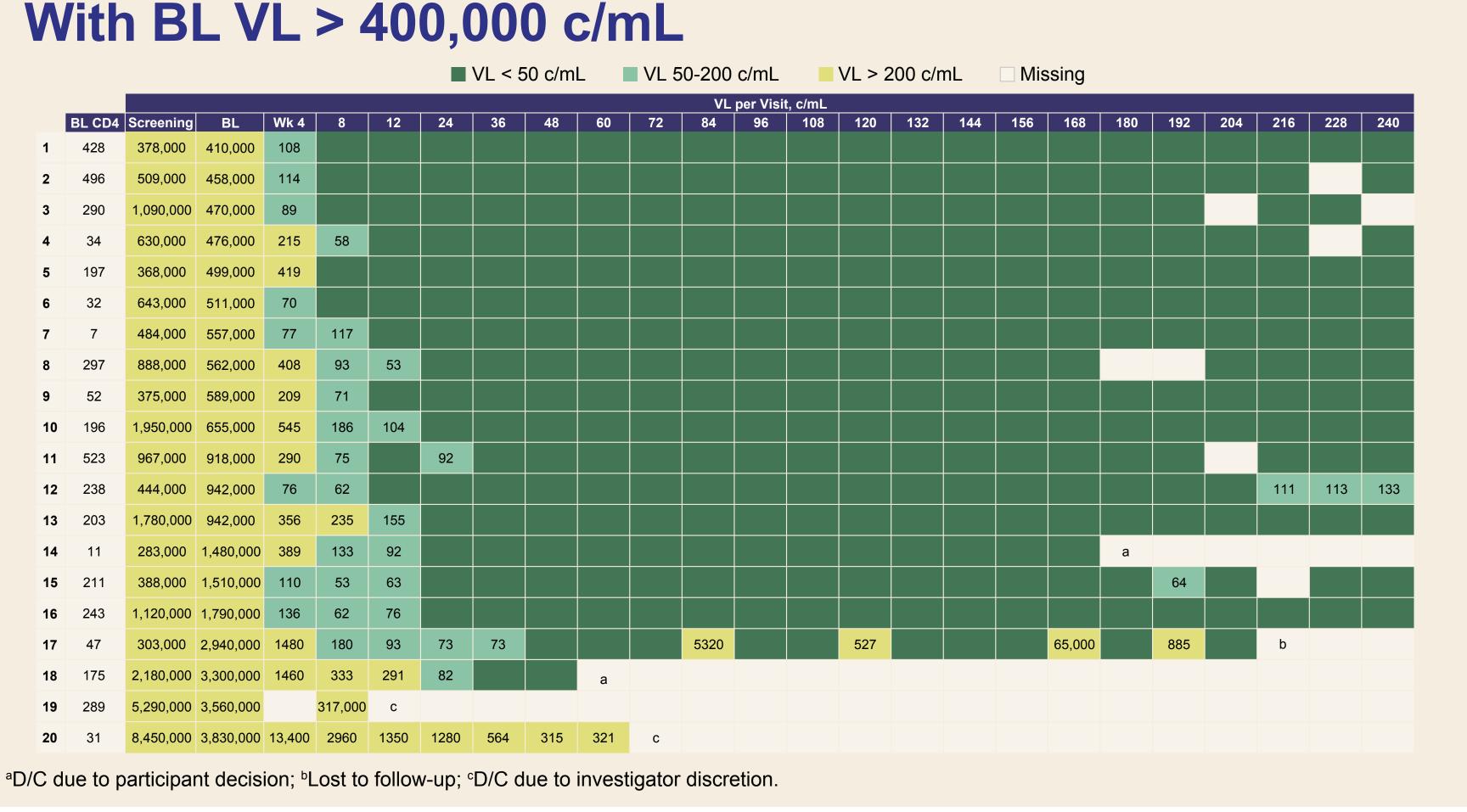
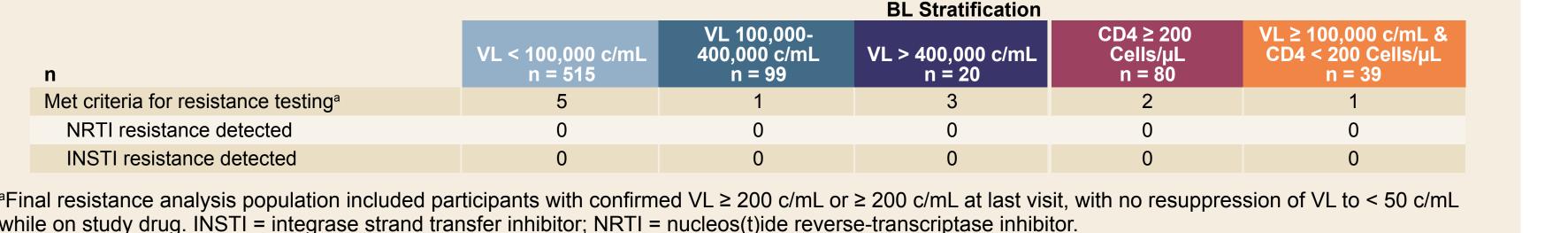
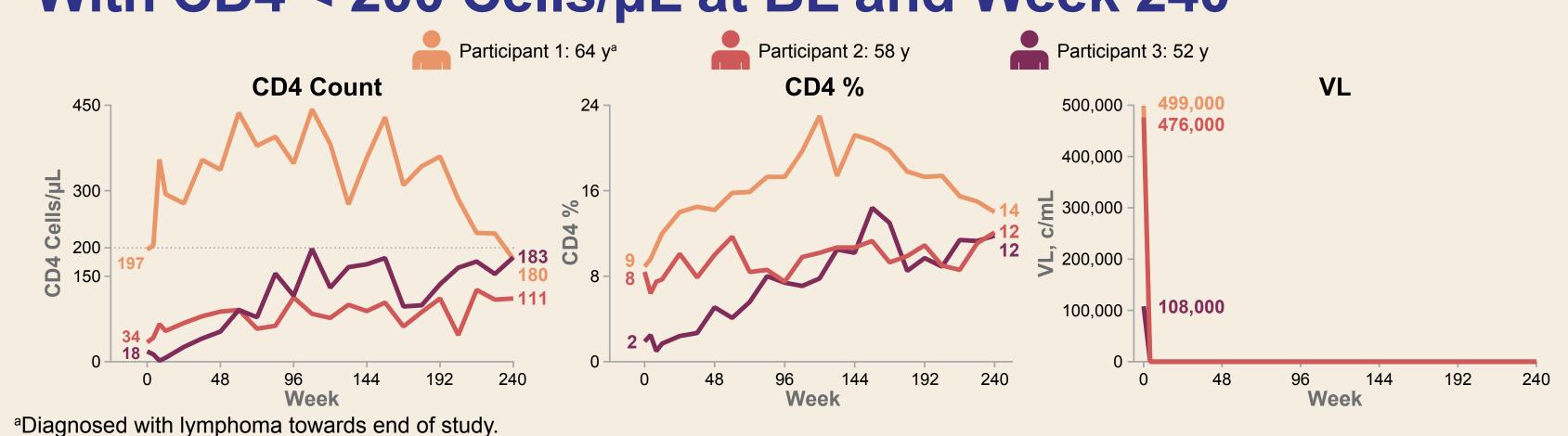


Table 2. Virologic Resistance Through Week 240



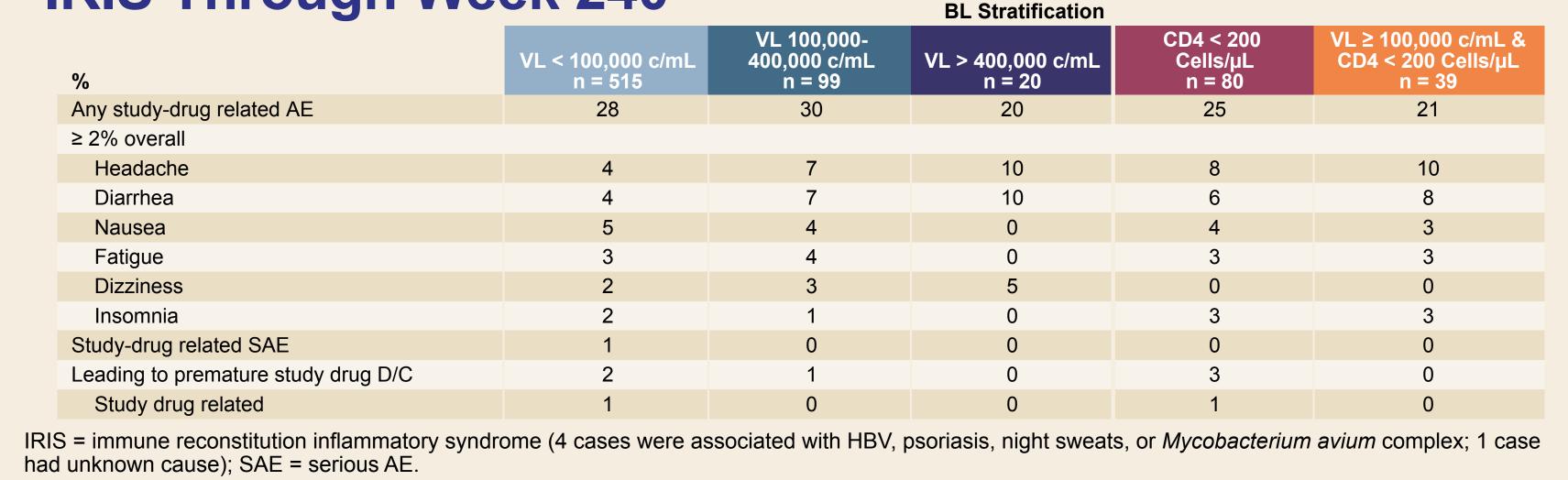
 None of the 9 participants in the final resistance analysis population developed treatment-emergent resistance to any component of B/F/TAF

Figure 5. Characteristics and Outcomes for Participants With CD4 < 200 Cells/µL at BL and Week 240



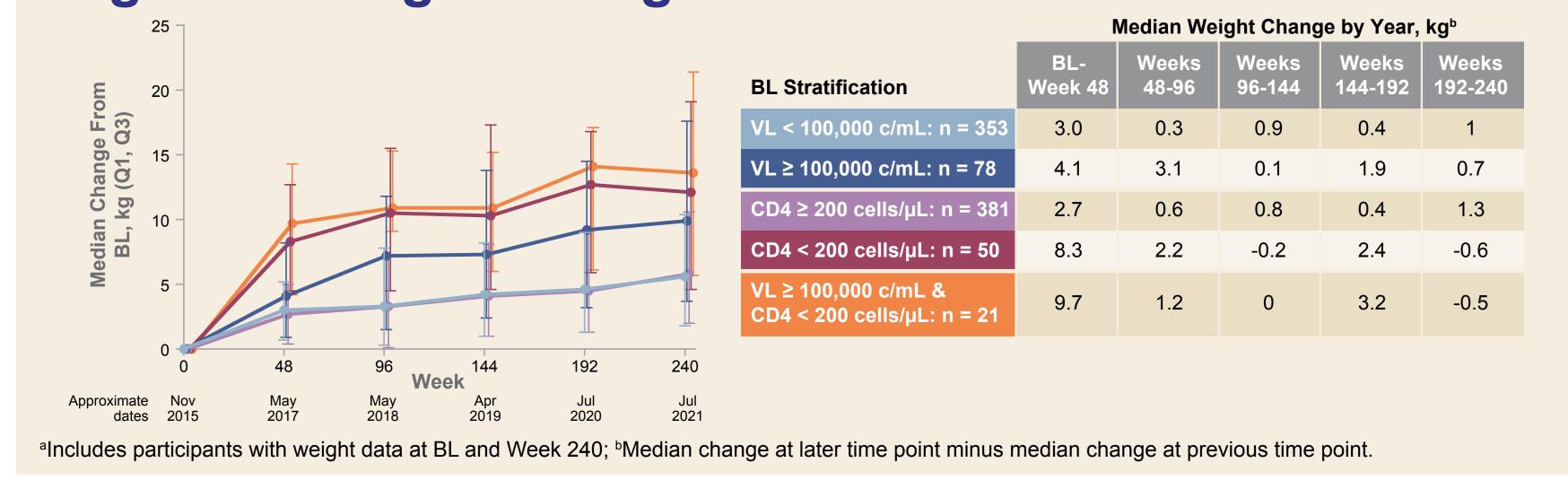
◆3/80 participants with BL CD4 < 200 cells/μL had CD4 < 200 cells/μL at Week 240 despite VL suppression by Week 4, which was maintained through Week 240

Table 3. Study Drug-Related AEs and Incident Cases of IRIS Through Week 240



- ◆ The most common study drug-related AEs were nausea, headache, and diarrhea; there were no drug-related SAEs in the high VL or low CD4 subgroups
- ◆ There was 1 study drug-related SAE (chest pain) leading to D/C in the VL < 100,000 c/mL subgroup and none in the high VL subgroups
- ♦ 5 cases of IRIS were reported: all had BL VL < 100,000 c/mL, 2 had CD4 < 200 cells/μL, and all occurred within the first 48 weeks and resolved with treatment

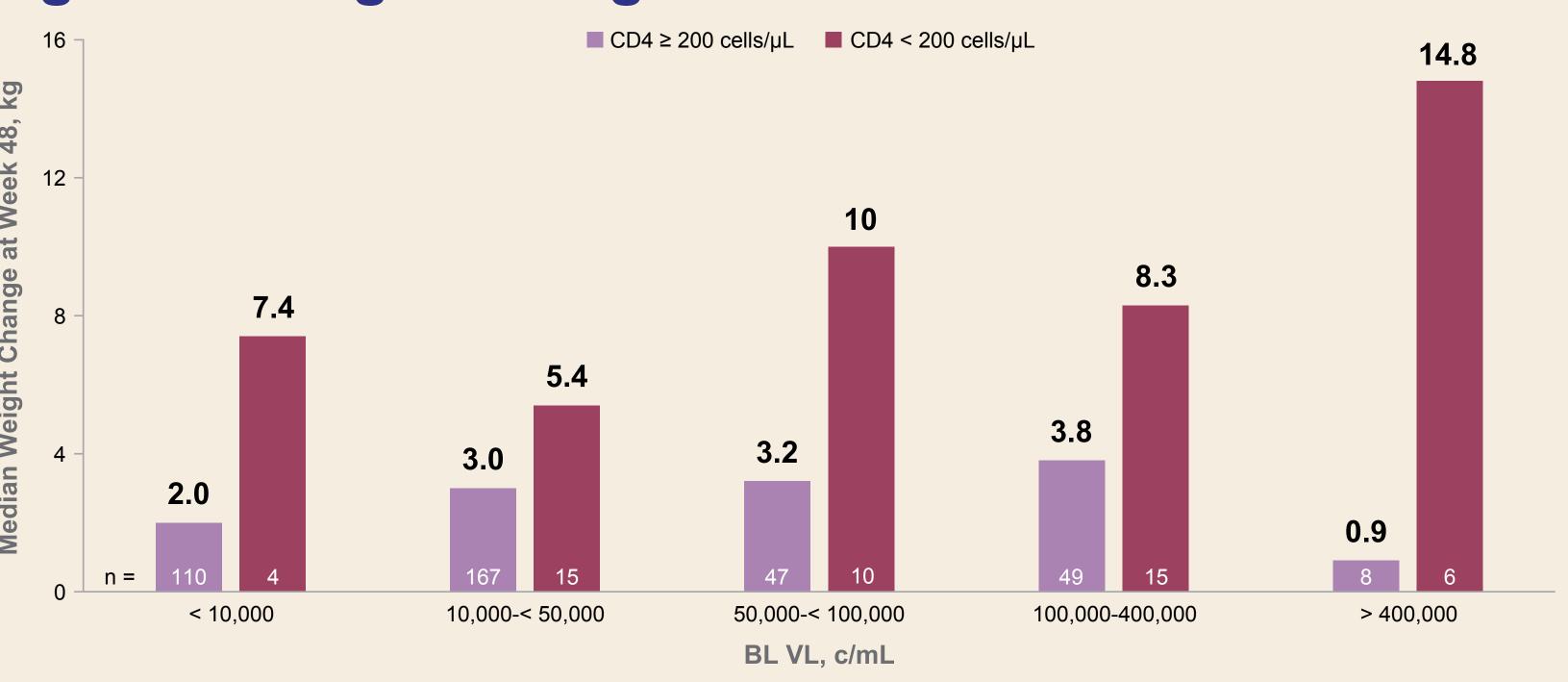
Figure 6. Weight Changes From Baseline^a



At Week 48:

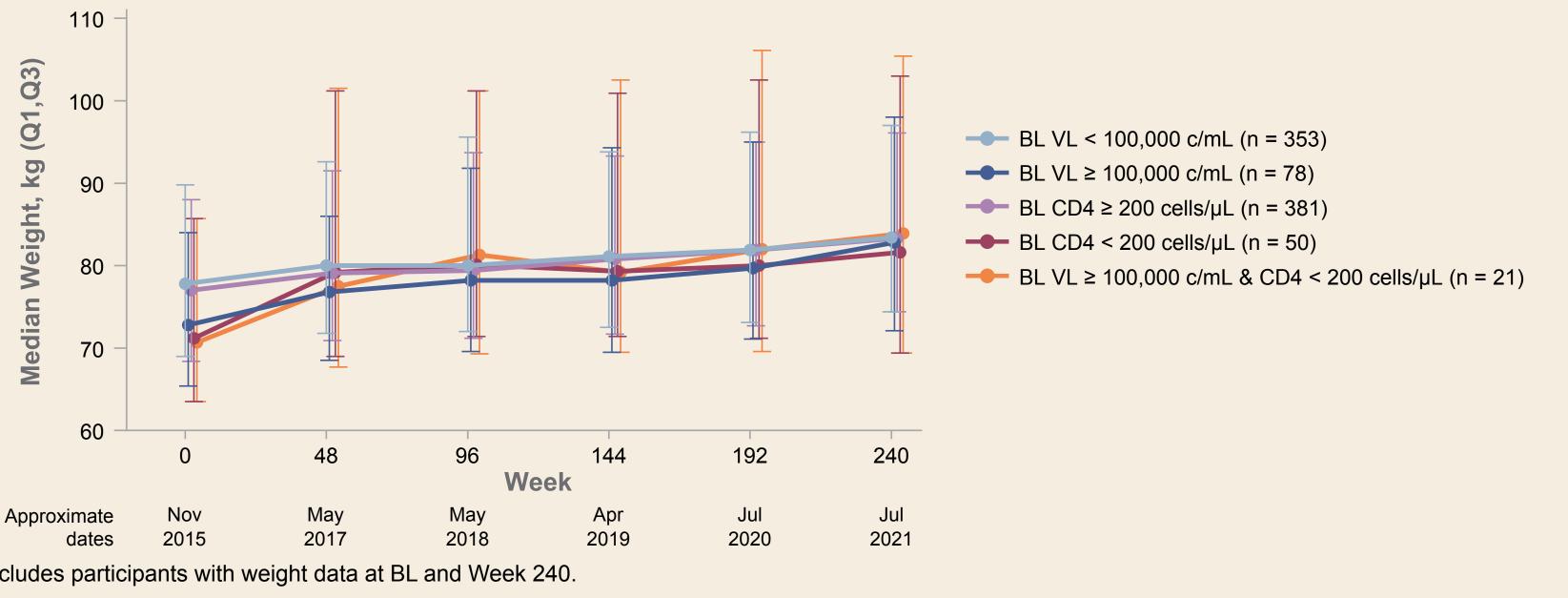
- People with BL VL ≥ 100,000 c/mL experienced more weight change than those with VL < 100,000 (4.1 vs 3.0 kg [P < 0.05])
- Those with BL CD4 < 200 cells/µL experienced more weight change than those with CD4 ≥ 200 (8.3 vs 2.7 kg [P < 0.001])
- Similarly, those with both VL ≥ 100,000 and CD4 < 200 at BL experienced more weight change than those with VL < 100,000 (9.7 vs 3.0 kg [P < 0.001])
- At Week 240, all groups with BL VL ≥ 100,000 c/mL had more cumulative weight change than those with BL VL < 100,000 (median 9.9 kg vs 5.6 kg [P < 0.001])

Figure 7. Weight Changes From Baseline at Week 48



In an additional analysis examining weight change at Week 48 by finer categories of VL, participants with BL VL < 10,000 c/mL and CD4 ≥ 200 cells/ μ L had less weight change than those with BL CD4 < 200 (2.0 vs 8.3 kg [P < 0.001]), BL VL ≥ 50,000 (2.0 vs 4.0 kg [P < 0.001]), and both BL CD4 < 200 and VL ≥ 50,000 (2.0 vs 10.0 kg [P < 0.001])

Figure 8. Actual Weight Over Time^a



- ♦ BL weights were significantly lower in participants with BL VL ≥ vs < 100,000 c/mL (72.8 vs 77.8 kg [P < 0.01]) and in those with BL CD4 < vs ≥ 200 cells/µL (71.2 vs 77.0 kg [P < 0.05])
- At Week 240, subgroups had comparable median actual weights

Conclusions

- ◆ In adults with HIV who started on an initial regimen of B/F/TAF and continued through 5 years of follow-up, this subgroup analysis stratified by BL VL and CD4 count demonstrated:
- High rates of virologic suppression, CD4 recovery, and no treatment-emergent resistance
- 16/20 participants with BL VL > 400,000 c/mL achieved VL < 200 c/mL by Week 8
- 77/80 participants with BL CD4 < 200 cells/μL had CD4 ≥ 200 cells/μL at Week 240
- Similar study drug-related AEs among subgroups, with < 1% of study drug-related AEs leading to D/C
 Greater median weight changes in the first year for participants with
- low CD4 and/or high VL at BL, consistent with a return-to-health phenomenon, and similar median actual weights at Year 5 among VL/CD4 subgroups
- These outcomes provide additional evidence that B/F/TAF is safe and shows durable efficacy for a broad range of PWH, including those with advanced disease at initial presentation

References: 1. Clinical Info HIV.gov. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV; 1/20/22; 2. EACS: European AIDS Clinical Society. Guidelines Version October 2021; 3. Saag MS, et al. *JAMA*. 2020;324:1651-69; 4. Darcis G, et al. *Sci Rep*. 2018;8:8594; 5. Komninakis S. *AIDS Res Hum Retroviruses*. 2018;34:128-31; 6. Lin K-Y, et al. *PLoS One*. 2017;12:e0179870; 7. Rava M, et al. *PLoS One*. 2021;16:e0249864; 8. Gallant J, et al. *Lancet*. 2017;390:2063-72; 9. Orkin C, et al. *Lancet*. HIV 2020;7:e389-400; 10. Sax PE, et al. *Lancet*. 2017;390:2061. Scan using the IDV Acknowledgments: We extend our thanks to the participants, their partners and families, and all GS-US-380-1489 and GS-US-380-1490 investigators. Special

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