



B/F/TAF Five-Year Outcomes in Treatment-Naïve Adults

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Introduction

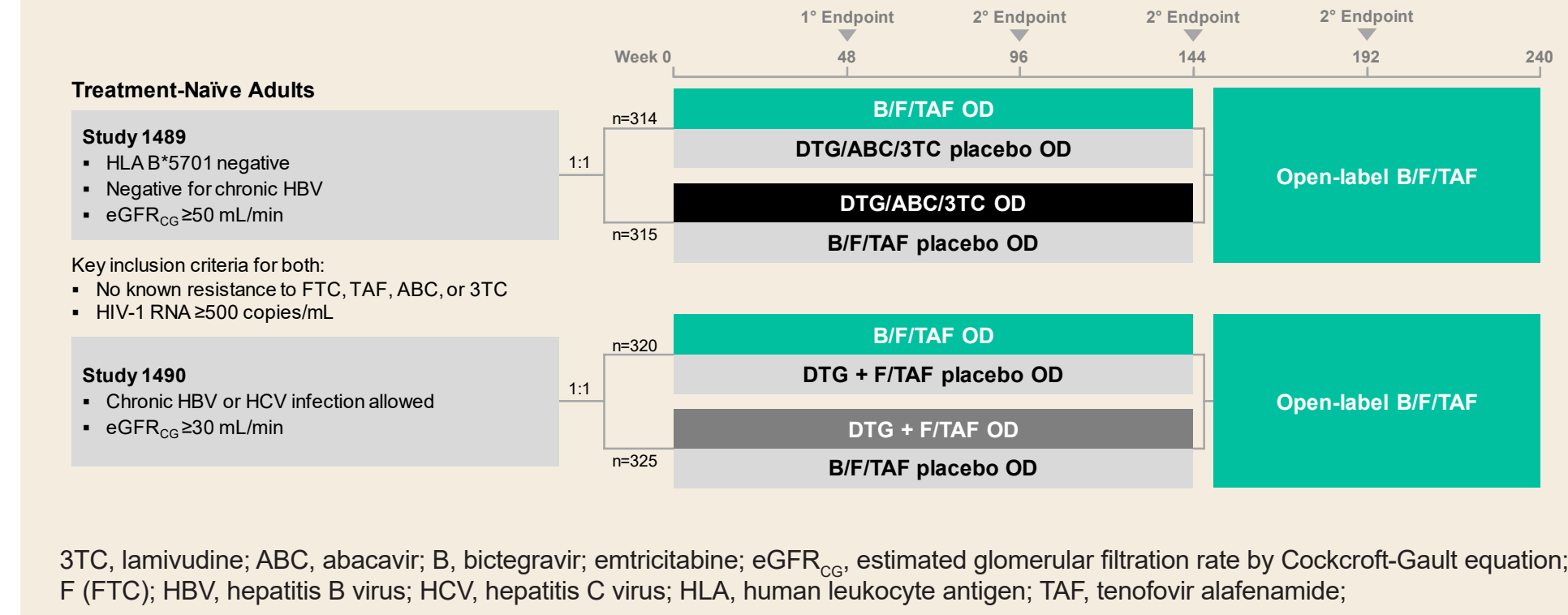
- B/F/TAF, the single-tablet coformulation of bictegravir (B; BIC), emtricitabine (F; FTC), and tenofovir alafenamide (TAF) is a guidelines-recommended regimen for people living with HIV¹⁻³
- B/F/TAF has a high barrier to resistance, favourable drug-drug interaction profile, and ability to be given once daily without food restrictions
- Efficacy and tolerability through Week 144 have been demonstrated in two Phase 3 studies (GS-US-380-1489 [NCT02607930] and GS-US-380-1490 [NCT02607956]) of B/F/TAF compared with 3-drug dolutegravir (DTG)-containing regimens in treatment-naïve adults⁴⁻⁸
- All participants who completed 144 wk of the blinded treatment phase were given the opportunity to participate in an open-label extension (OLE) for an additional 96 wk

Objectives

- To assess 5-year outcomes (144 wk of blinded treatment plus 96 wk in OLE [aka Week 240]) from Studies 1489 and 1490
- The present analysis focuses on those participants originally randomised to B/F/TAF to gain further insight into long term tolerability and efficacy

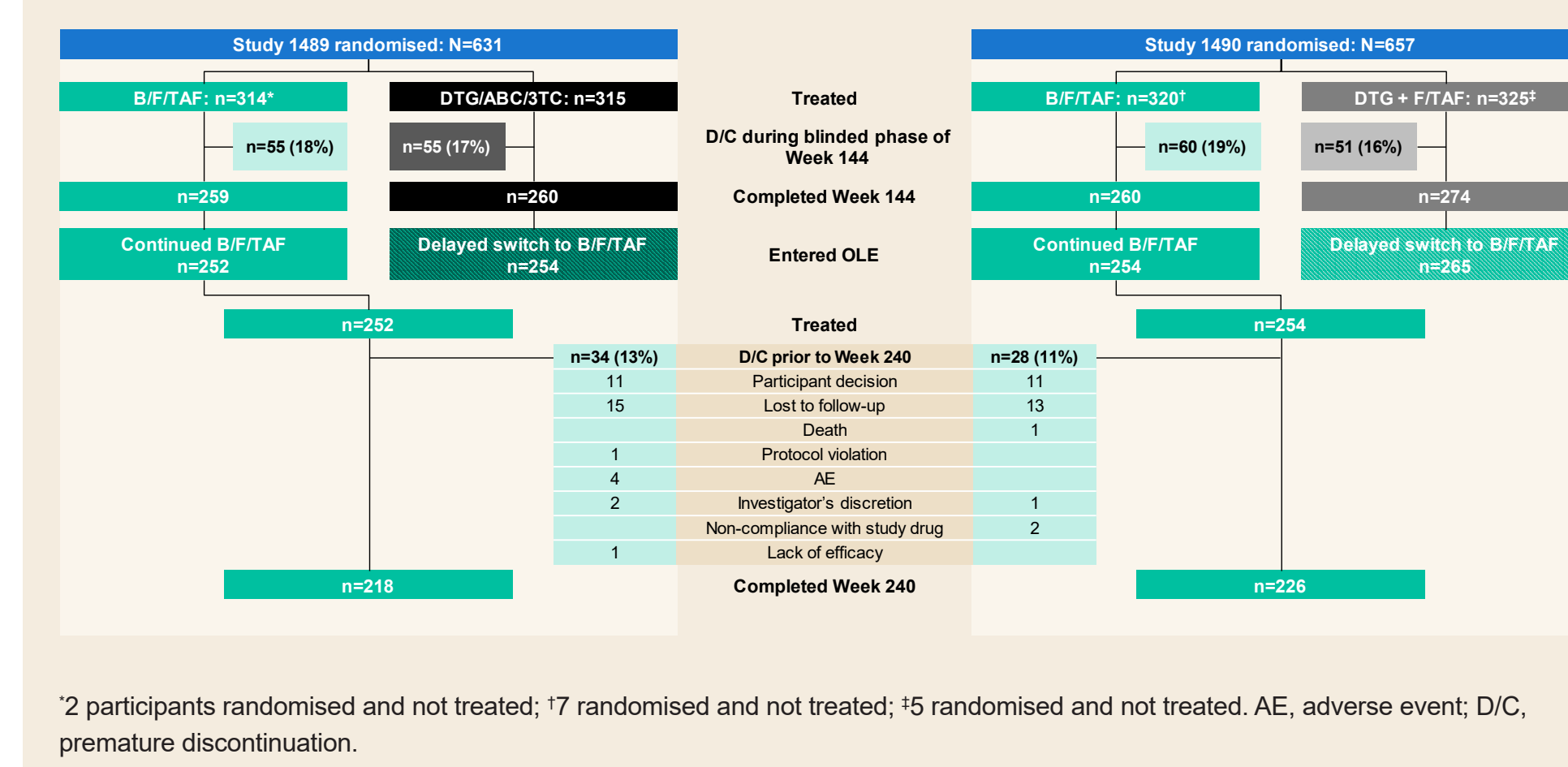
Methods

Study Designs: Randomised, Double Blind, Active Controlled



Results

Participant Disposition From Baseline to Week 240

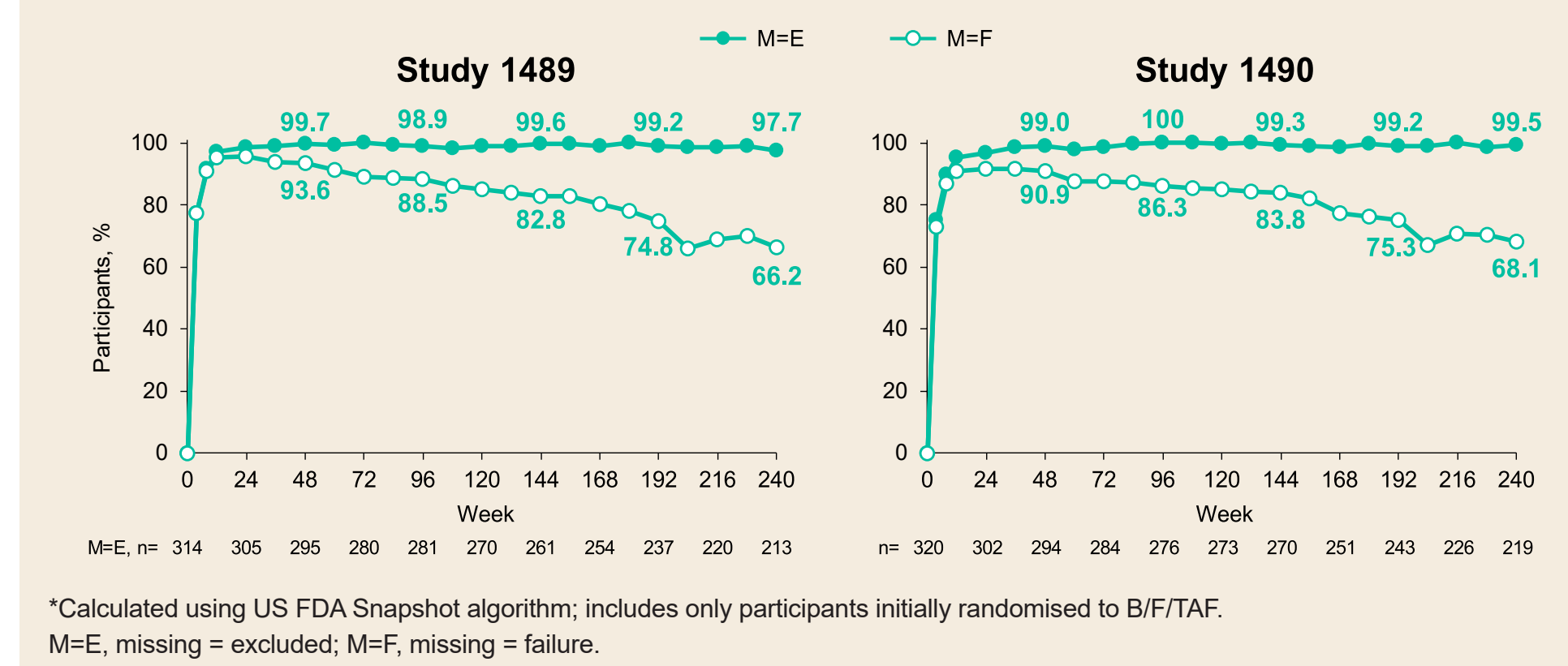


Characteristics at B/F/TAF Start*

	Study 1489 B/F/TAF n=314	Study 1490 B/F/TAF n=320
Median age, y (range)	31 (18–71)	33 (18–71)
Female sex at birth, n (%)	29 (9)	40 (13)
Race/ethnicity, n (%)		
Black or African descent	114 (37)	97 (30)
Hispanic/Latin ethnicity	72 (23)	83 (26)
Median body weight, kg (IQR)	77 (68, 88)	76 (68, 87)
Median HIV-1 RNA, log ₁₀ copies/mL (IQR)	4.4 (4.0, 4.9)	4.4 (4.0, 4.9)
HIV-1 RNA >100,000 copies/mL, n (%)	53 (17)	66 (21)
Median CD4 cells/μL (IQR)	443 (299, 590)	440 (289, 591)
CD4 count <200 cells/μL, n (%)	36 (11)	44 (14)
Asymptomatic HIV infection, n (%)	286 (91)	286 (89)
Median eGFR _{CG} , mL/min (IQR)	126 (108, 146)	120 (101, 142)

*Includes only participants initially randomised to B/F/TAF. CD4, cluster of differentiation-4; IQR, interquartile range.

Virologic Outcomes Through Week 240 HIV-1 RNA <50 Copies/mL*



- Efficacy was ≥98% (M=E) after Week 48 at each study visit through Week 240 in both studies for all participants
- Among those with baseline CD4 <200 cells/μL from the pooled studies, 98% (49/50) had HIV-1 RNA <50 copies/mL at Week 240
- Median CD4 changes from B/F/TAF start to Week 240, cells/μL (IQR): Study 1489: +313 (179, 475); Study 1490: +331 (215, 467)

Results (cont'd)

Virologic Resistance Through Week 240

Participants, n	Study 1489 B/F/TAF n=314	Study 1490 B/F/TAF n=320
Met criteria for resistance testing*	1	8
NRTI resistance detected	0	0
INSTI resistance detected	0	0

*Final resistance analysis population included participants with confirmed HIV-1 RNA ≥200 copies/mL at last visit, with no suppression of HIV-1 RNA to <50 copies/mL while on study drug; includes only participants initially randomised to B/F/TAF. INSTI, integrase strand transfer inhibitor; NRTI, nucleos(t)ide reverse-transcriptase inhibitor.

- No resistance to any components of B/F/TAF occurred in any group of the final resistance analysis population

Adverse Events Through Week 240*

Participants, %	Study 1489 B/F/TAF: n=314	Study 1490 B/F/TAF: n=320
Any AE	97	93
>10% in either study		
Diarrhoea	19	24
Headache	16	21
Nasopharyngitis	18	19
URTI	17	17
Syphilis	18	16
Arthralgia	14	14
Back pain	15	13
Cough	13	13
Nausea	14	11
Fatigue	13	9
Anxiety	14	8
Insomnia	11	11
Influenza	8	13
Pain in extremity	8	10
Rash	12	6
Oropharyngeal pain	10	8
Hypertension	10	7

*Includes only participants initially randomised to B/F/TAF. URTI, upper respiratory tract infection.

Adverse Events Through Week 240* Study Drug-Related AEs

Participants, %	Study 1489 B/F/TAF: n=314	Study 1490 B/F/TAF: n=320
Any study drug-related AE ¹	32	24
Grade 3–4	1	2
>5% in either study		
Diarrhoea	6	3
Headache	5	5
Nausea	5	3

AEs Leading to D/C*

Study 1489 B/F/TAF: n=4/314 (1%)	Study 1490 B/F/TAF: n=6/320 (2%)
Intervertebral discitis (Day 1366)	Chest pain (Day 1)
Toxicity to various agents (Day 1549)	Abdominal distension (Day 1)
Obesity (Day 1634)	Sleep disorder, dyspepsia, and tension headache (Day 15); depressed mood and insomnia (Day 63)
COVID-19 (Day 1748)	Cardiac arrest (Day 28)
	Paranoia (Day 299)
	Depression (Day 337)

*Includes only participants initially randomised to B/F/TAF; ¹Mostly Grade 1 and rarely led to D/C; ²Italics indicate AEs considered study drug related by investigator; red shading indicates events that occurred after Week 192; each row represents 1 participant.

- Few participants (n=5) experienced a study drug-related AE that led to D/C

Laboratory Abnormalities Through Week 240*

Participants, %	Study 1489 B/F/TAF n=314	Study 1490 B/F/TAF n=320
Any Grade 3/4 laboratory abnormality	34	32
Grade 3/4 laboratory abnormalities ≥3% in either group		
Increased creatine kinase [†]	12	10
Increased LDL (fasting)	6	5
Increased AST [‡]	5	3
Increased amylase [§]	4	4
Increased ALT [‡]	3	4
Decreased neutrophils	3	4

*Includes only participants initially randomised to B/F/TAF; [†]Elevations asymptomatic, no cases of myositis, commonly occurred postexercise, and not deemed clinically significant; [‡]No cases of drug-related hepatitis; [§]1 case of drug-attributed pancreatitis on Day 572 (resolved Day 574); participant did not D/C study drug. ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDL, low-density lipoprotein.

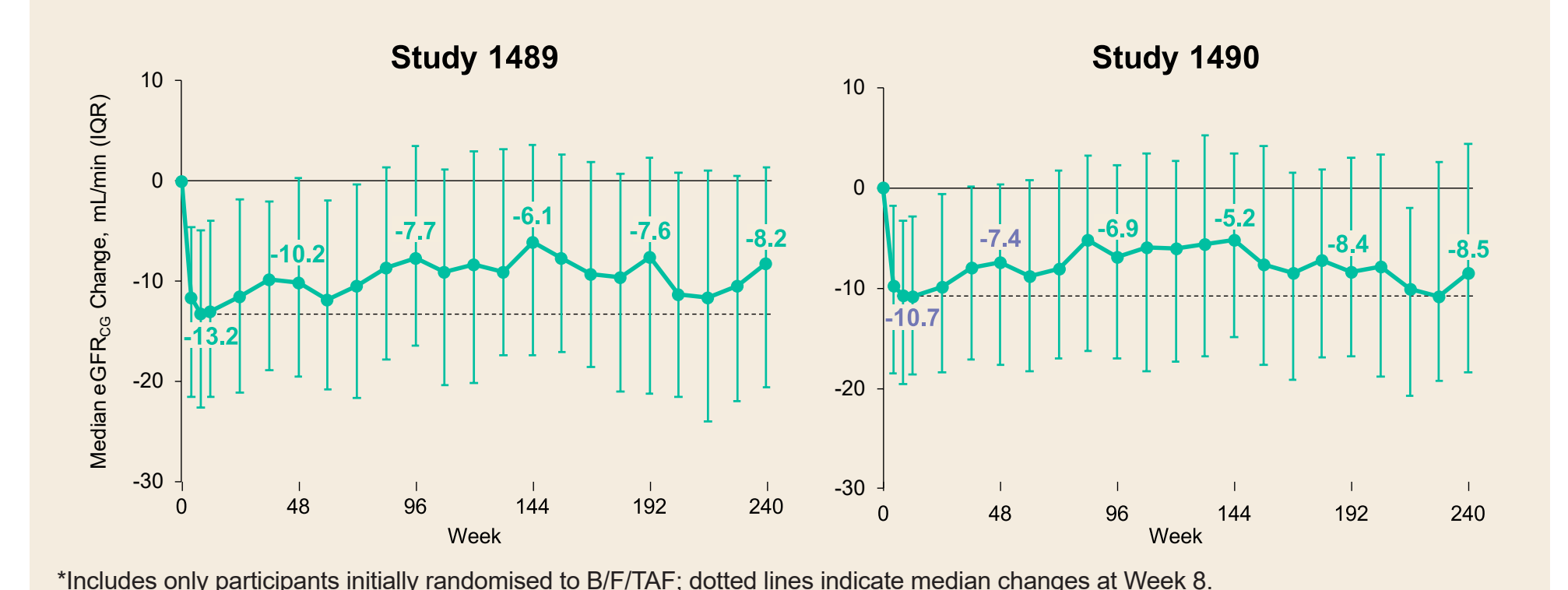
Conclusions

- In treatment-naïve people living with HIV through 5 years of follow-up among those originally randomised to B/F/TAF, we observed:
 - High rates of virologic suppression with no treatment-emergent resistance in the final resistance analysis population
 - ≤1% occurrence of study drug-related AEs leading to discontinuation and no renal-related discontinuation
 - Stable eGFR_{CG} after organic cation transporter-2–related initial declines and no reported cases of proximal renal tubulopathy
 - Small changes in fasting lipids, with stable TC:HDL ratios and few participants initiating lipid-lowering agents
 - Median cumulative weight gain of 6.1 kg; ~3 kg in first 48 wk, followed by ~0.3–1.5 kg/y, consistent with data from previous studies in treatment-naïve populations¹¹⁻¹⁶
 - Weight gains after Week 48 are consistent with what is seen in the general US population¹⁰
 - Minimal impact on longitudinal trends of spine and hip BMD from baseline, with mean decreases that did not exceed 0.29% at Week 240
- These results add further evidence to the long-term tolerability and efficacy of B/F/TAF

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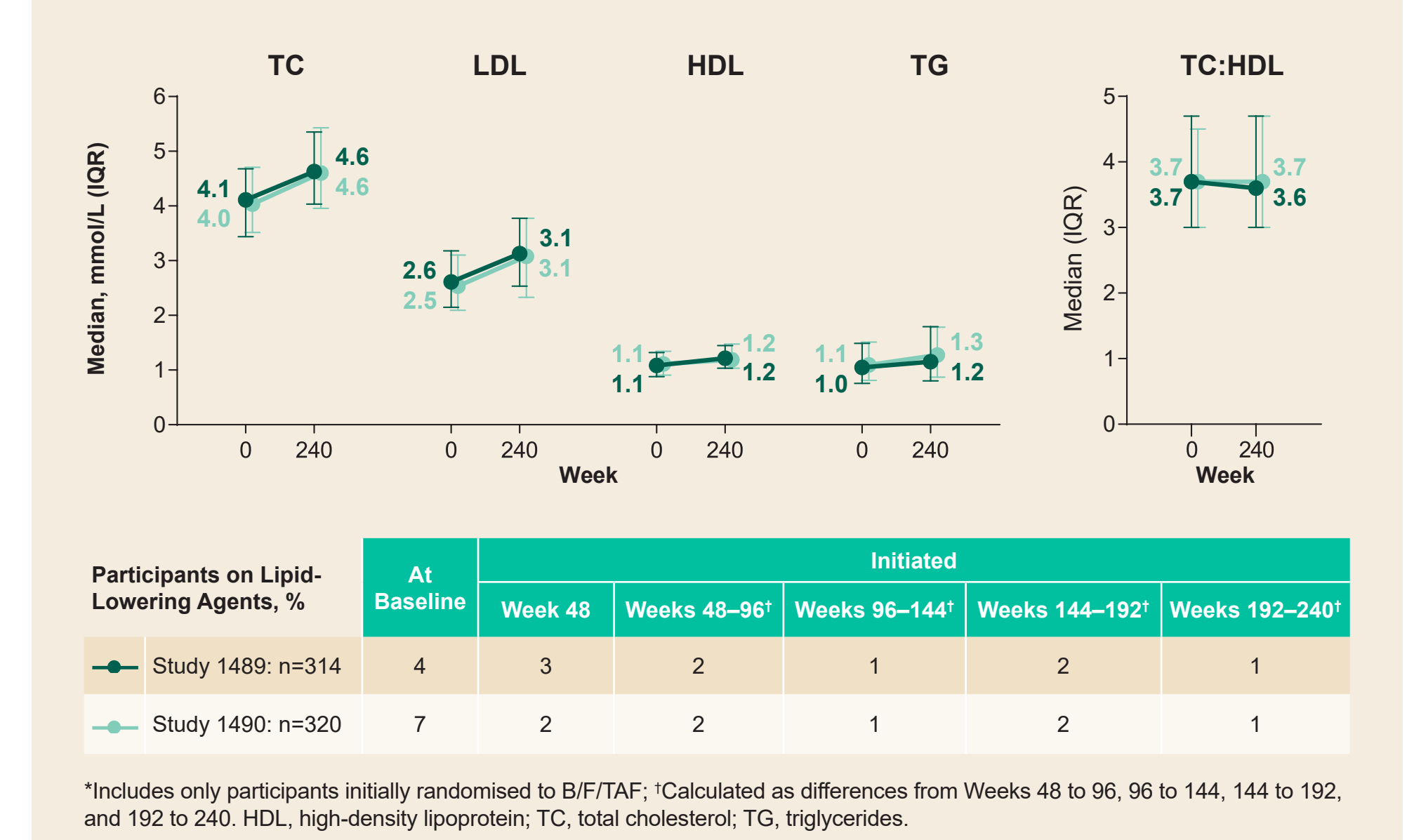
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eGFR Changes From Baseline Through Week 240*



- No reported cases of proximal renal tubulopathy or D/C due to renal AEs were observed with B/F/TAF
- Initial decline followed by stable eGFR_{CG} is consistent with the inhibition of tubular secretion of creatinine by BIC via organic cation transporter-2⁹

Fasting Lipids Through Week 240*



- Small changes in lipids were observed among participants randomised to B/F/TAF over 5 years, with stable TC:HDL ratios, and small numbers of participants who initiated lipid-lowering agents between baseline and Week 240

Weight Changes From Randomised Phase Baseline Through Week 240*



- Median cumulative weight gain from baseline to Week 240 was 6.1 kg for participants initially randomised to B/F/TAF
- Weight gains after Week 48 are consistent with what is seen in the general US population¹⁰

Spine and Hip BMD Changes Through Week 240 Study 1489*

