Incidence of Metabolic Complications Among Treatment-naïve Adults Living With HIV-1 Randomized to B/F/TAF, DTG/ABC/3TC or DTG + F/TAF After 3 Years

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on behalf of the Study GS-US-380-1489 and GS-US-380-1490 study investigators

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Disclosures

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- Consultant for Gilead, Merck and ViiV

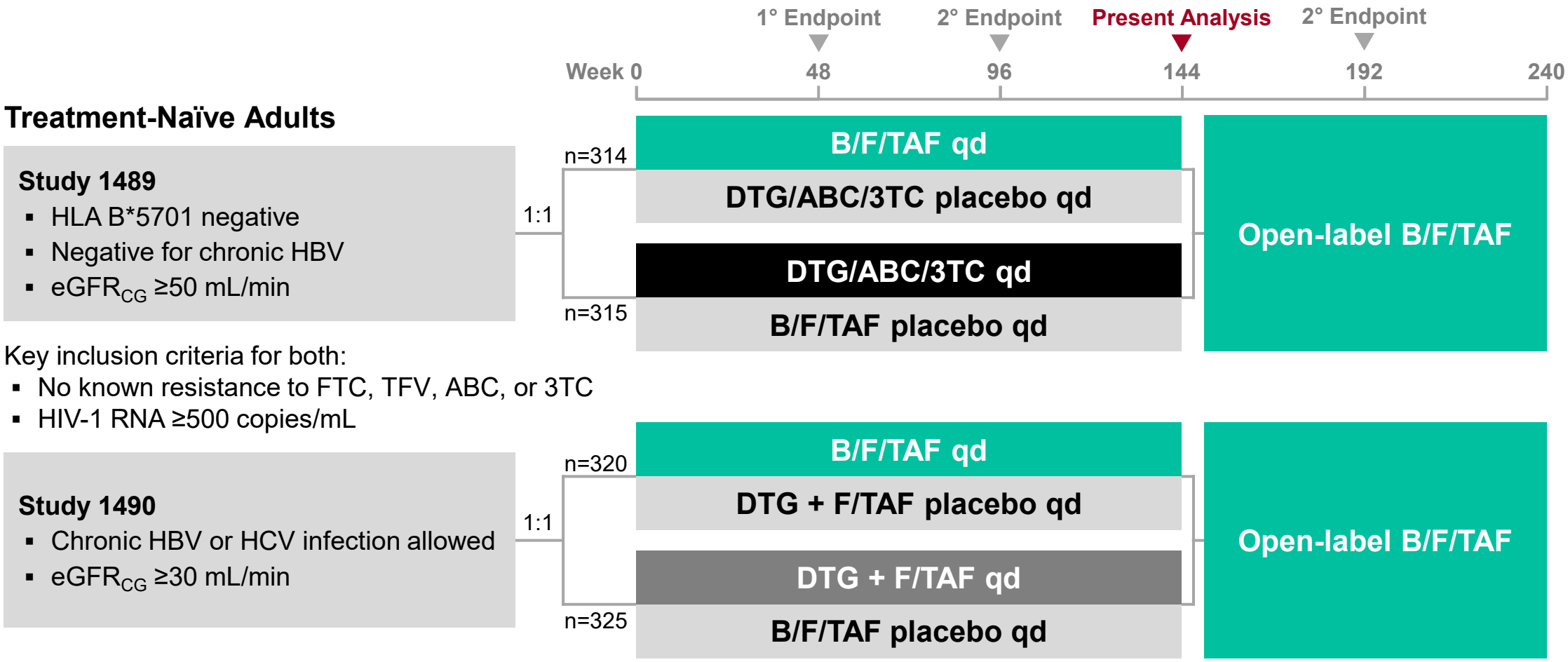
Introduction

- Metabolic complications, including cardiovascular disease, diabetes and dyslipidemia, are challenges to the long-term health of PWH
  - Cardiovascular disease and diabetes are reported at higher rates in PWH compared to the general population[1-2]
- Obesity is prevalent in the general population and in PWH and contributes to metabolic complications, including increased fasting lipids and glucose[3-7]
- Elevated lipids and glucose have been associated with some ARVs, including INSTIs, and may contribute to increased risk of comorbidities, including hypertension and type 2 diabetes[8-10]
- Here we present longer-term follow up on the incident events of **diabetes**, **hypertension**, **BMI change/categorical shifts** and **lipid changes** over 3 years of blinded treatment from two trials of PWH initiating antiretroviral therapy with an INSTI-based regimen

1. Noubissi EC, et al. Curr Diab Reb 2018;18:125; 2. Luo Q, et al. Journal of the IAS. HIVRP Virtual 2021;suppl 1:202; 3. WHO 2016. CDC and Prevention 2016; 4. Sax PE, et al. Clin Infect Dis 2020;71:1379-89; 5. Achhra AC, et al. HIV Med 2016;17:255-68; 6. Herrin M, et al. J Acquir Immune Defic Syndr 2016; 73:228-36; 7. Morse CG, et al. JAMA 2006;296:844-54; 8. Lagathu C, et al. Expert Opin Drug Saf 2019;18:829-40; 9. Galdamez R, et al. Open Forum Infect Dis 2019;6:ofz491; 10. Rebeiro PF, et al. Clin Infect Dis 2020 Sep 16;ciaa1403.
ARV, antiretroviral; BMI, body mass index; INSTI, integrase strand transfer inhibitor; PWH, people with HIV.

Methods

Study Designs: Randomized, Double Blind, Active Controlled



3TC, lamivudine; ABC, abacavir; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; DTG/ABC/3TC, dolutegravir/abacavir/lamivudine; $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault equation; HBV, hepatitis B virus; HCV, hepatitis C virus; HLA, human leukocyte antigen; TFV, tenofovir.

Methods

- Safety analysis set data* from Study 1489: B/F/TAF vs DTG/ABC/3TC and Study 1490: B/F/TAF vs DTG + F/TAF between November 2015 and May 2019 were reviewed
- Participants with reported adverse event terms of treatment-emergent metabolic comorbidities were defined by SMQ search lists and graded laboratory measurements from baseline to Week 144
  - **Diabetes Mellitus** defined by:
    - Hyperglycemia/new onset diabetes mellitus SMQ (Narrow Scope)
    - Fasting glucose
  - **Hypertension** defined by:
    - Hypertension SMQ
  - **BMI change** defined by:
    - Median BMI change
    - CDC-defined BMI categorical shifts
  - **Lipid changes** defined by:
    - Fasting lipid parameters (total cholesterol, LDL, HDL, triglycerides and TC:HDL)
- Subgroup analyses by sex at birth and race (Black vs Nonblack) were performed

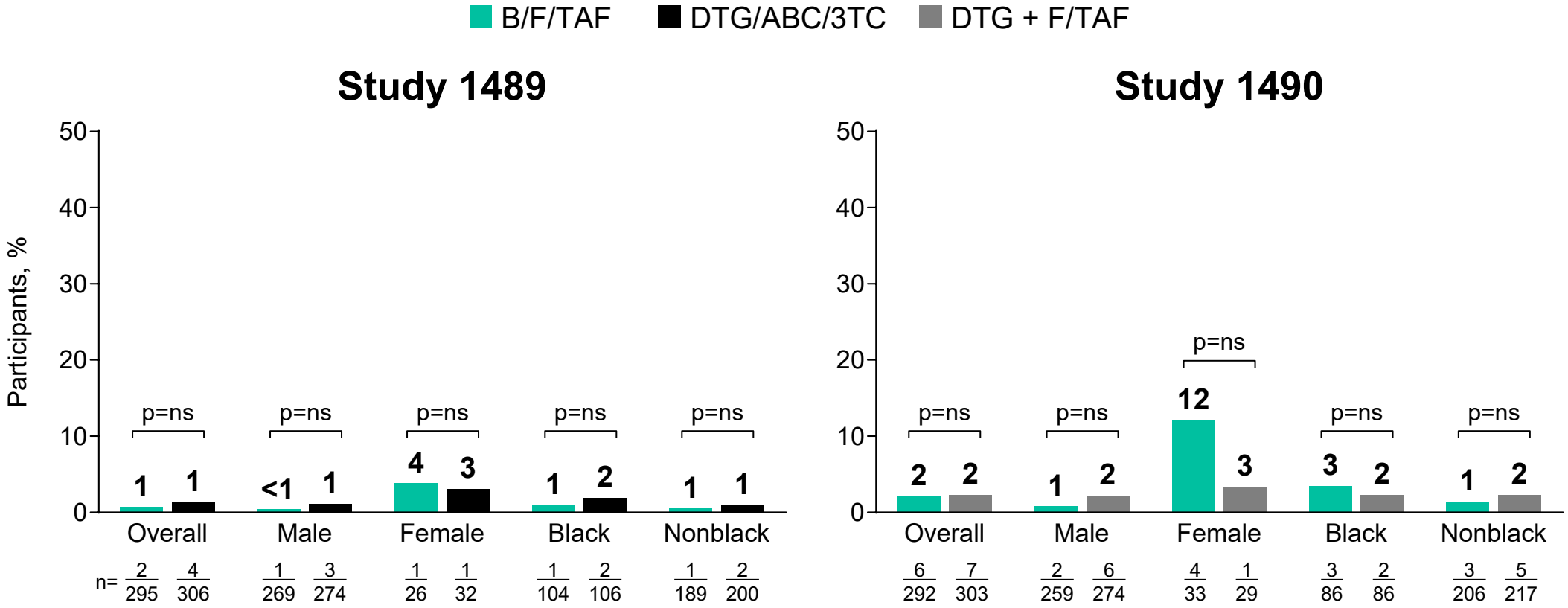
*Safety analysis data, participants grouped according to the ARV treatment they actually received and collected up to 30 days after last dose date.
HDL, high-density lipoprotein; LDL, low-density lipoprotein; SMQ, Standardized Medical Dictionary for Regulatory Activities (MedDRA) Query; TC, total cholesterol.

Baseline Characteristics

	Study 1489		Study 1490	
	B/F/TAF n=314	DTG/ABC/3TC n=315	B/F/TAF n=320*	DTG + F/TAF n=325
Median age, y (range)	31 (18–71)	32 (18–68)	33 (18–71)	34 (18–77)
Male sex at birth, %	91	90	88	89
Race/ethnicity, %				
Black or African descent	36	36	30	31
Hispanic/Latinx	23	21	26	25
Median HIV-1 RNA, log_{10} copies/mL (IQR)	4.4 (4.0, 4.9)	4.5 (4.0, 4.9)	4.4 (4.0, 4.9)	4.5 (4.0, 4.8)
Median CD4 cells/μL (IQR)	443 (299, 590)	450 (324, 608)	440 (289, 591)	441 (297, 597)
Asymptomatic HIV infection, %	91	91	89	89
Median $eGFR_{CG}$, mL/min (IQR)	126 (108, 146)	123 (107, 144)	120 (101, 142)	121 (103, 145)
Median BMI, kg/m^2 (IQR)	25 (22, 29)	25 (23, 29)	25 (22, 28)	25 (22, 28)
Diabetes, %	6	3	7	7
Hypertension, %	11	13	18	19

*Postbaseline data unavailable for 6 participants. CD4, cluster of differentiation-4; IQR, interquartile range.

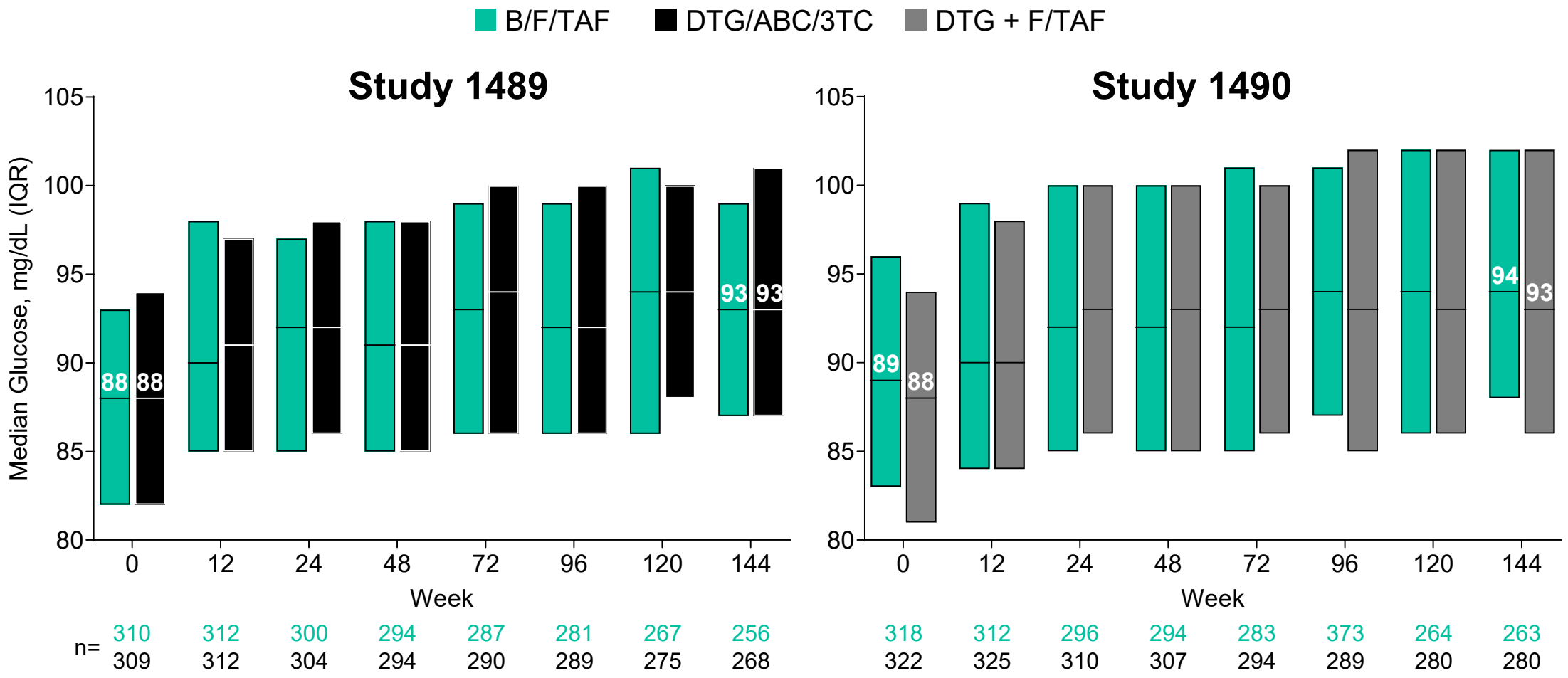
Treatment-Emergent Diabetes* Through Week 144



- Treatment-emergent diabetes events occurred at low rates in both studies (1–2% of overall population)
  - Subgroup analyses showed similar findings when evaluating participants by sex at birth or race

*Excluding those with medical history of diabetes; p-values from Fisher exact test to compare treatment groups; diabetes events defined using search list "hyperglycemia/new onset diabetes mellitus (SMQ) — narrow scope" in MedDRA version 23.1. ns, nonsignificant (p≥0.05).

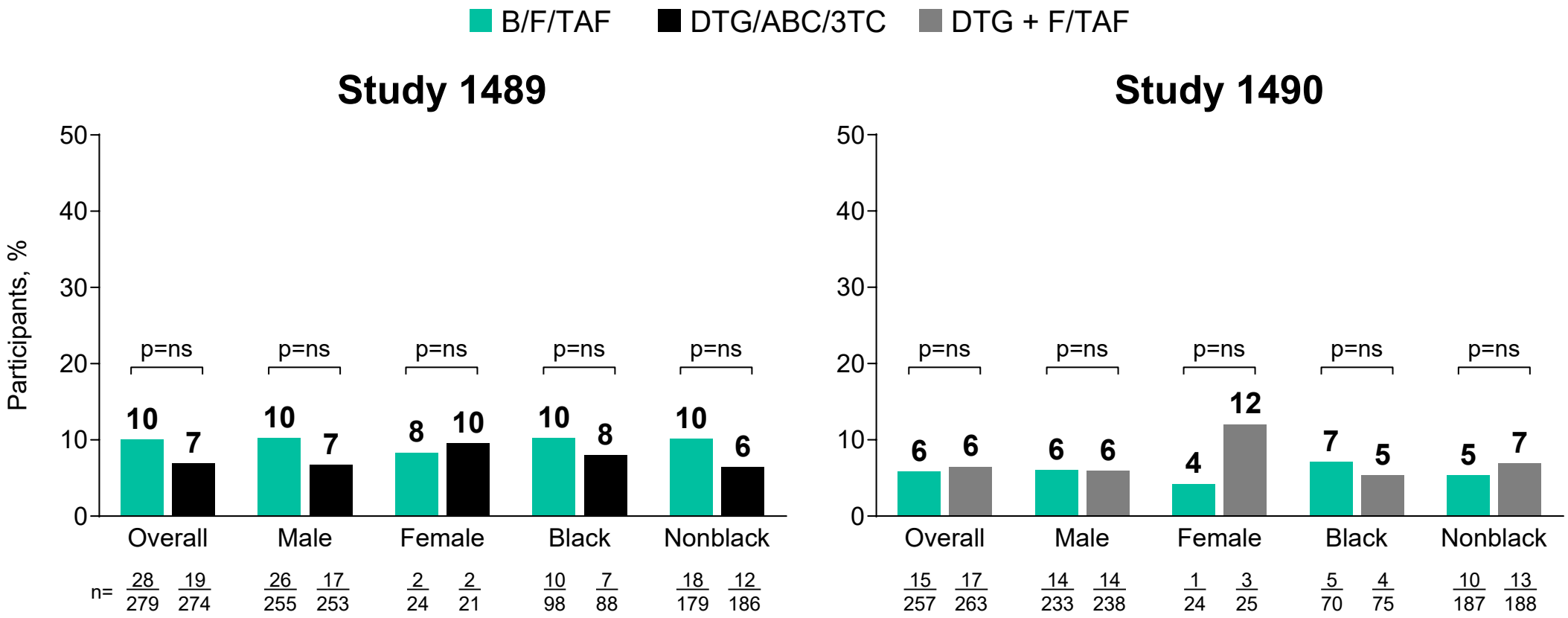
Fasting Blood Glucose Through Week 144: Overall*



- Median fasting blood glucose changes at Week 144 were not significant when compared between groups (Study 1489: p=0.64, 1490: p=0.96†)

*Includes those with diabetes at baseline; †p-values from 2-sided Wilcoxon rank sum test to compare 2 treatment groups in each study.

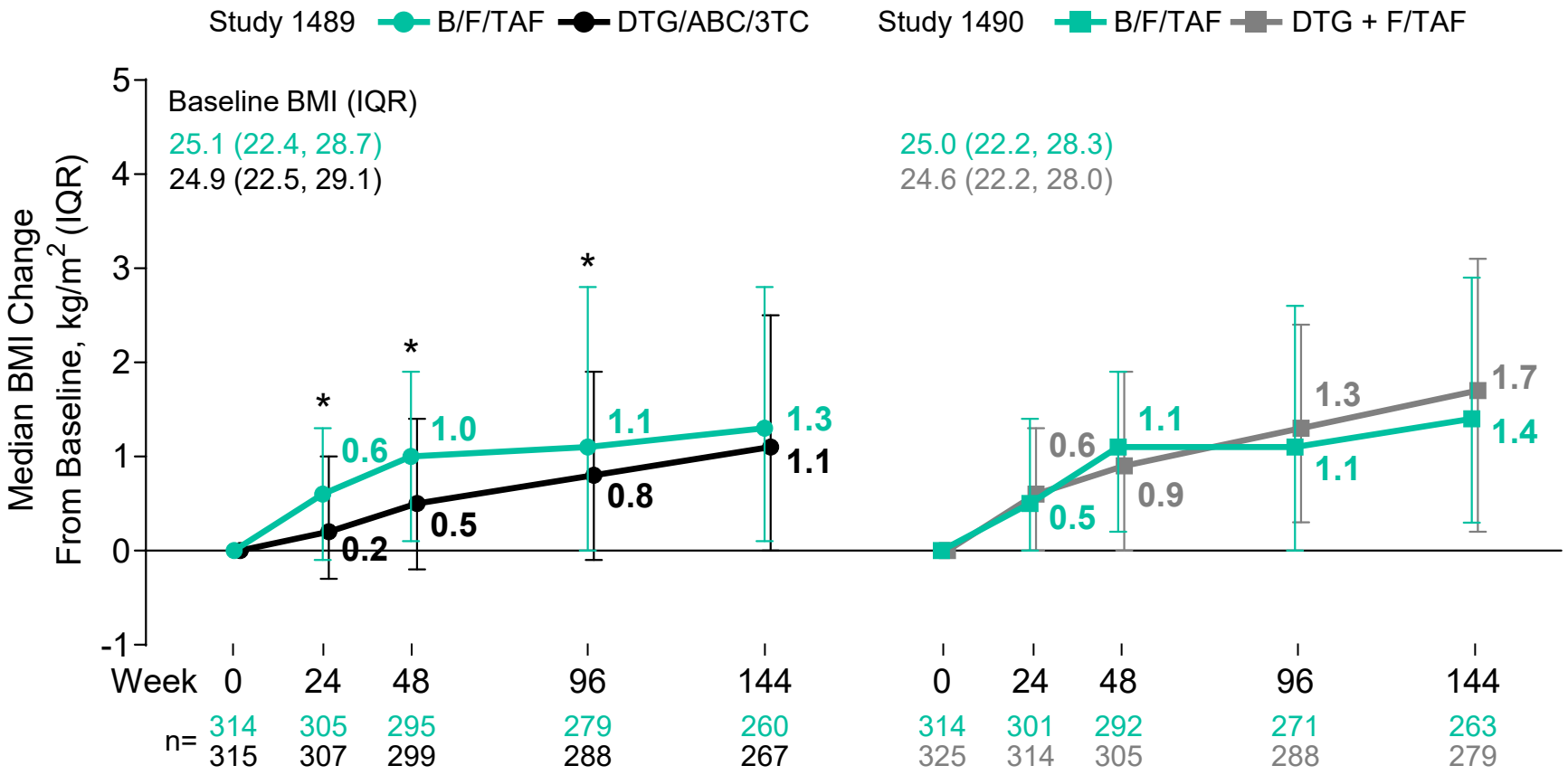
Treatment-Emergent Hypertension* Through Week 144



- Treatment-emergent hypertension events occurred ≤10% in both studies in the overall population
- Subgroup analyses showed similar findings when evaluating participants by sex at birth or race

*Excluding those with medical history of hypertension; p-values from Fisher exact test to compare treatment groups; hypertension events defined using search list "hypertension (SMQ)" in MedDRA version 23.1; ns, nonsignificant (p≥0.05).

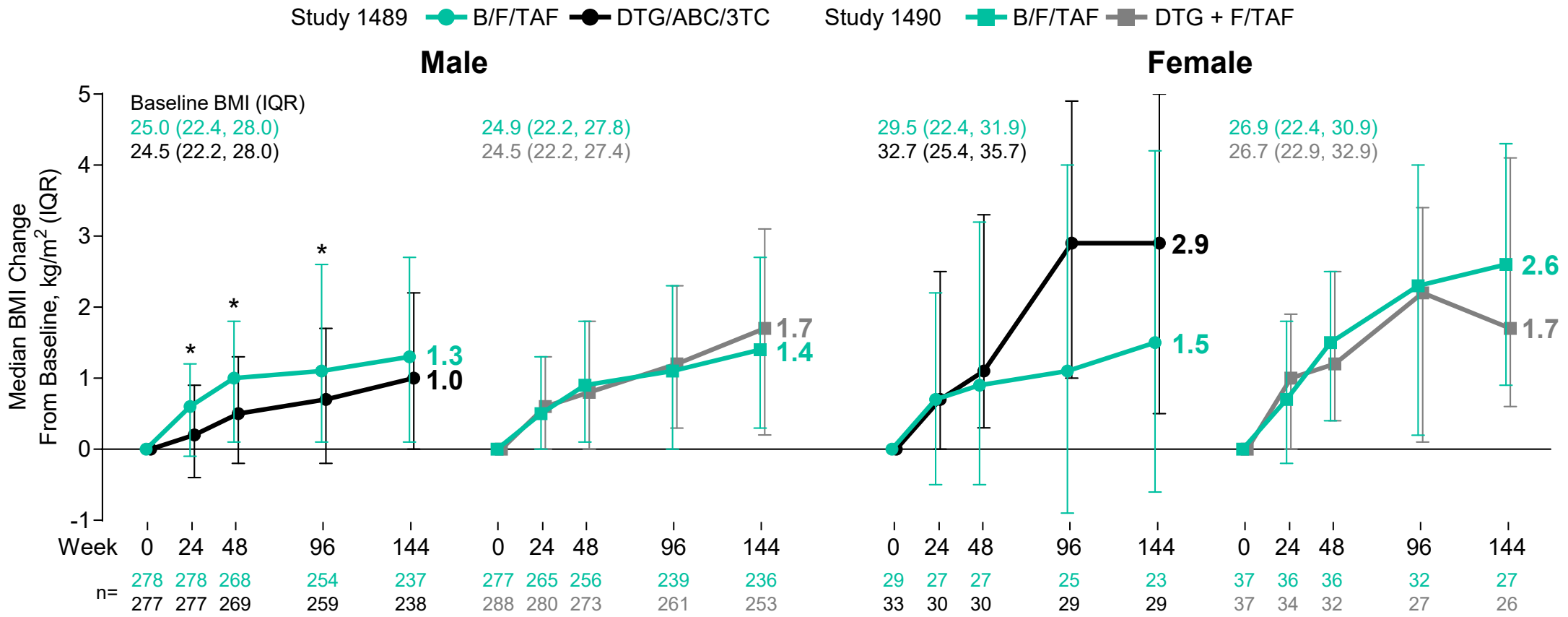
Median BMI Change Through Week 144: Overall



- Median BMI change was significantly different in Study 1489 at Weeks 24, 48 and 96 between the treatment groups, but was not significant at Week 144
- No significant differences observed at Weeks 24, 48, 96 or 144 in Study 1490

*p<0.05, from 2-sided Wilcoxon rank sum test to compare 2 treatment groups in each study.

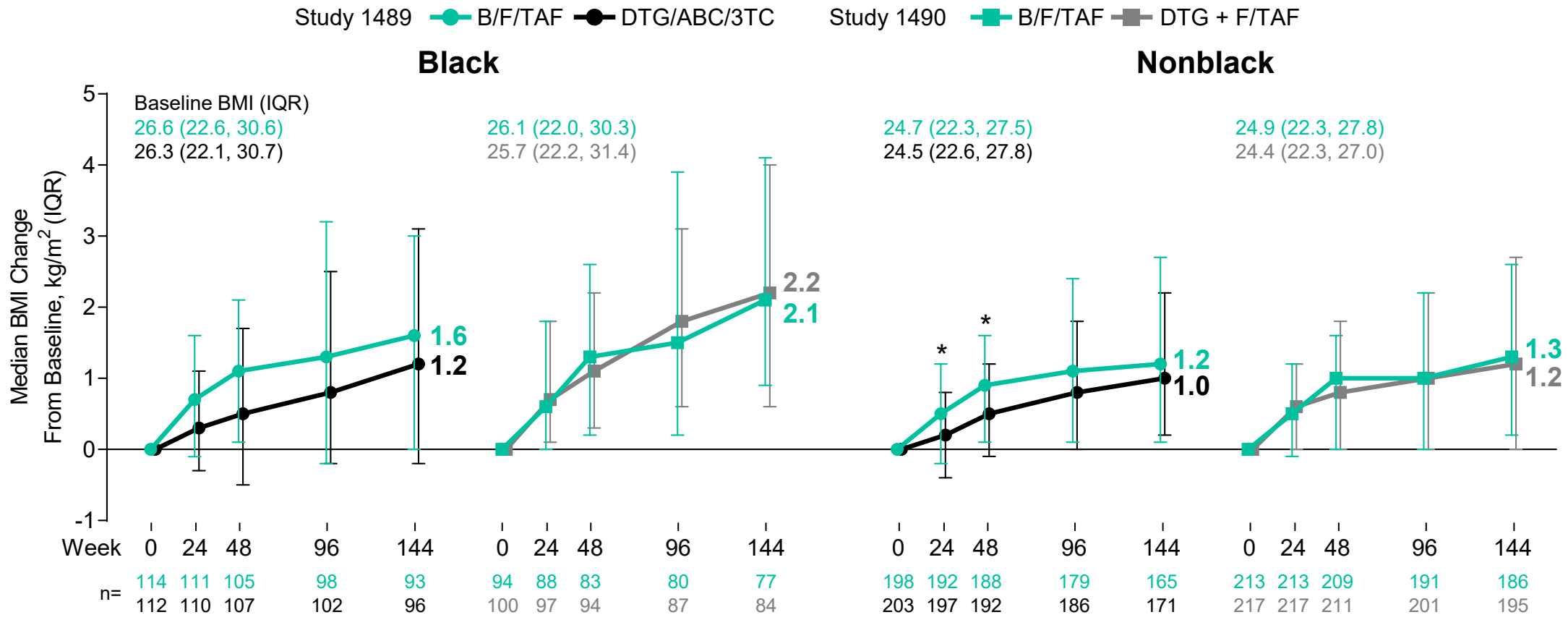
Median BMI Change from Baseline at Week 144: Sex at Birth



- Among males, median BMI change was significantly different between the treatment groups in Study 1489 at Weeks 24, 48 and 96, but was not significant at Week 144
- No significant treatment differences observed for BMI change among males in Study 1490, or among females in either study
- Analysis of females is limited by small number of participants

*p<0.05, from 2-sided Wilcoxon rank sum test to compare 2 treatment groups in each study.

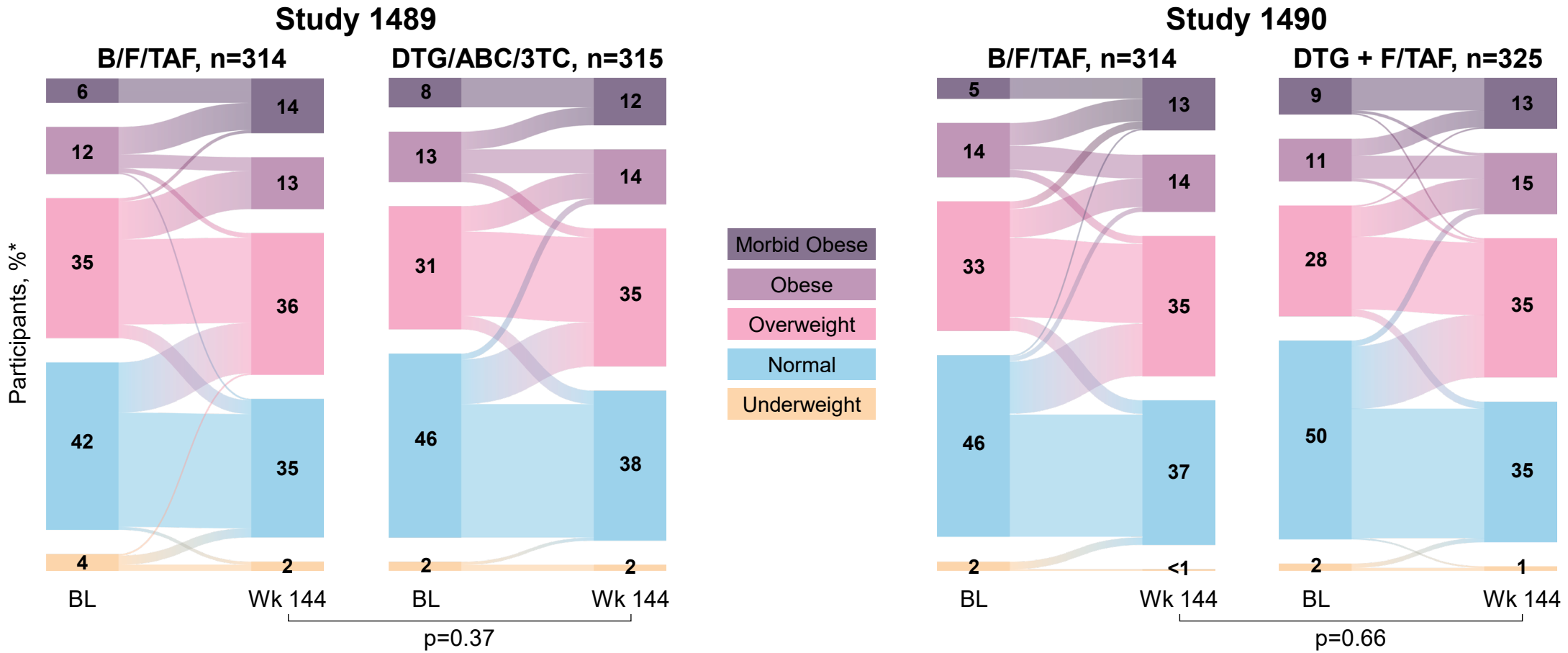
Median BMI Change from Baseline at Week 144: Race



- No significant treatment differences observed for BMI change at Week 144 among Black vs Nonblack participants in Study 1489 or 1490

*p<0.05, from 2-sided Wilcoxon rank sum test to compare 2 treatment groups in each study.

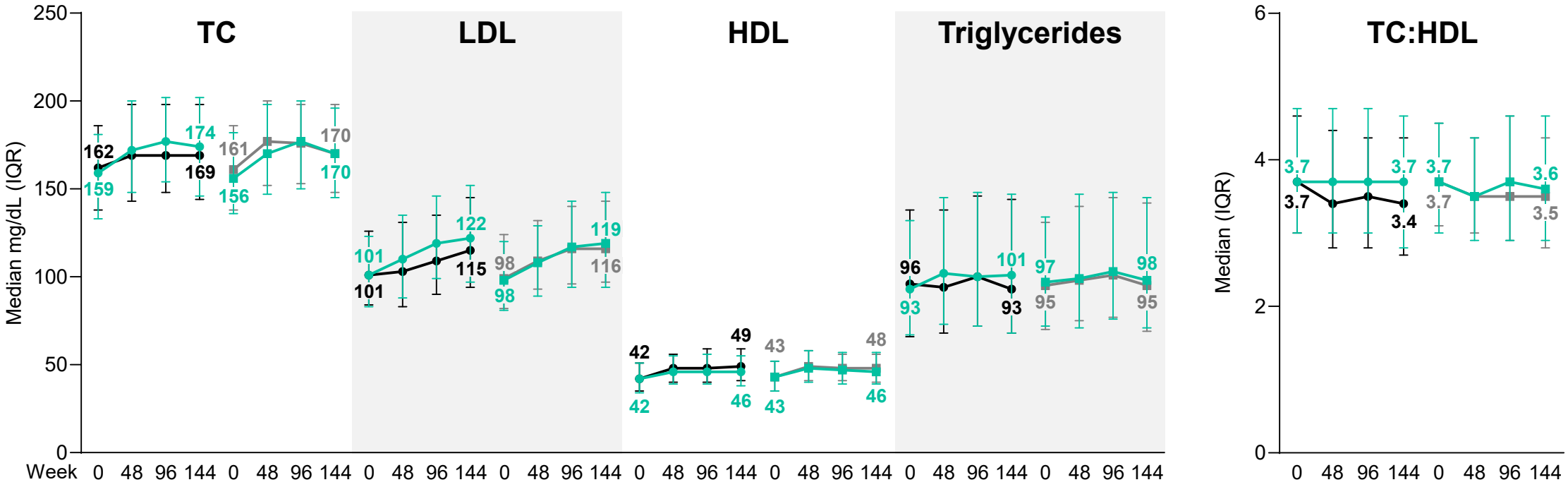
BMI Categorical Shifts, Baseline and Week 144: Overall



- Majority of participants remained in the same BMI category from baseline to Week 144
- No significant differences seen across categories at Week 144 between treatment arms in both studies
- No difference observed by subgroup analyses of sex at birth or race (Black vs Nonblack)

*Denominator for percentage was the number of participants with nonmissing values at Wk 144 in a given treatment group. Underweight: <18.5 kg/m^2; Normal: ≥18.5–<25 kg/m^2; Overweight: ≥25–<30 kg/m^2; Obese: ≥30–<35 kg/m^2; Morbid obesity: ≥35 kg/m^2. p-values were from rank analysis of covariance adjusted for baseline BMI category for treatment comparison.

Fasting Lipid Changes Through Week 144



Participants, %		Study 1489 B/F/TAF: n=314	Study 1489 DTG/ABC/3TC: n=315	Study 1490 B/F/TAF: n=320	Study 1490 DTG + F/TAF: n=325
Initiated lipid-lowering agents	Week 48	3	3	2	2
	Week 48–96*	2	1	2	2
	Week 96–144*	1	1	1	1

- Graded abnormalities in fasting lipids were reported for generally similar percentages of participants in each group
  - Modestly larger increase in TC and LDL as well as smaller reductions in TC:HDL ratio for those receiving B/F/TAF as compared to DTG/ABC/3TC

*Calculated as the difference from Week 48 to Week 96, and Week 96 to Week 144.

Conclusions

- No significant differences were observed when comparing B/F/TAF, DTG/ABC/3TC or DTG + F/TAF for incident diabetes or hypertension
  - Low rates of incident diabetes and/or hypertension occurred in Studies 1489 and 1490 through Week 144
- BMI increased over time in all groups; however, BMI change or categorical distribution at Week 144 did not differ by treatment regimen in either study
  - Study 1489: There was greater short-term increase in BMI with B/F/TAF vs DTG/ABC/3TC through week 96, but no difference at week 144
  - Study 1490: BMI change was not significantly different at any of the analyzed timepoints for participants randomized to B/F/TAF or DTG + F/TAF, including subgroup analyses by race and sex at birth
- Fasting lipid changes were small and few participants initiated lipid-lowering therapy

Acknowledgments

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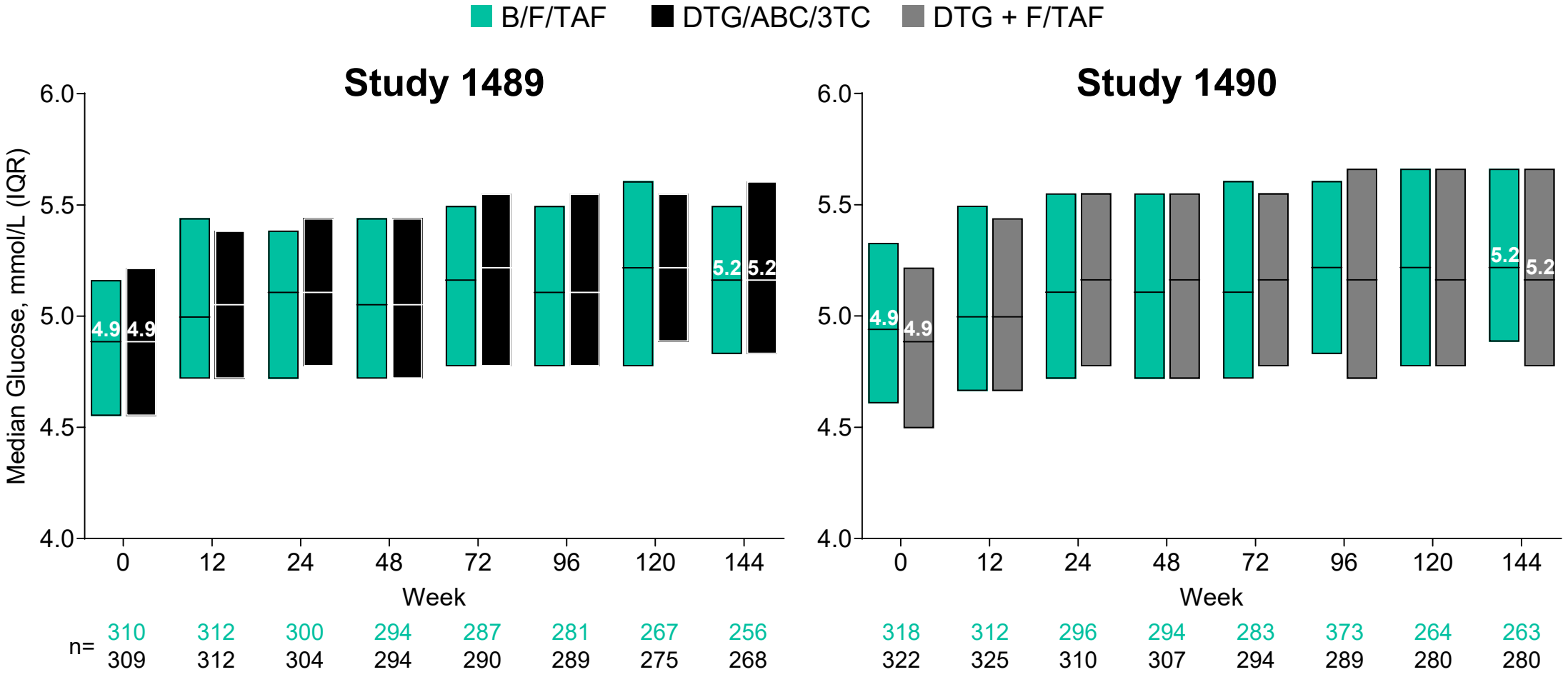
Backups

Fasting Blood Glucose Through Week 144: Overall*

mmol/L
x 0.05551

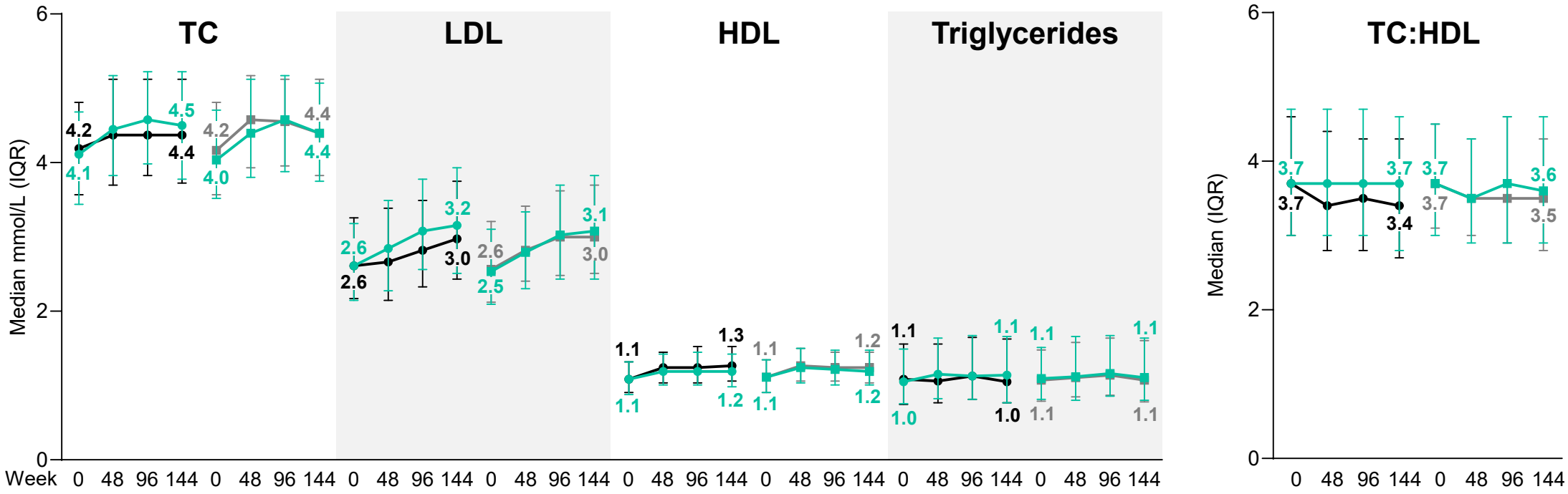


- Median fasting blood glucose changes at Week 144 were not significant when compared between groups (Study 1489: p=0.64, 1490: p=0.96†)

*Includes those with diabetes at baseline; †p-values from 2-sided Wilcoxon rank sum test to compare 2 treatment groups in each study.

Fasting Lipid Changes Through Week 144

mmol/L
TC, LDL, HDL: x 0.02586
TG: x 0.01129



Participants, %		Study 1489		Study 1490	
		B/F/TAF: n=314	DTG/ABC/3TC: n=315	B/F/TAF: n=320	DTG + F/TAF: n=325
Initiated lipid-lowering agents	Week 48	3	3	2	2
	Week 48–96*	2	1	2	2
	Week 96–144*	1	1	1	1

- Graded abnormalities in fasting lipids were reported for generally similar percentages of participants in each group
  - Modestly larger increase in TC and LDL as well as smaller reductions in TC:HDL ratio for those receiving B/F/TAF as compared to DTG/ABC/3TC

*Calculated as the difference from Week 48 to Week 96, and Week 96 to Week 144.