Longer Term Efficacy and Safety of F/TAF and F/TDF For HIV PrEP: DISCOVER Trial Week 96 Results

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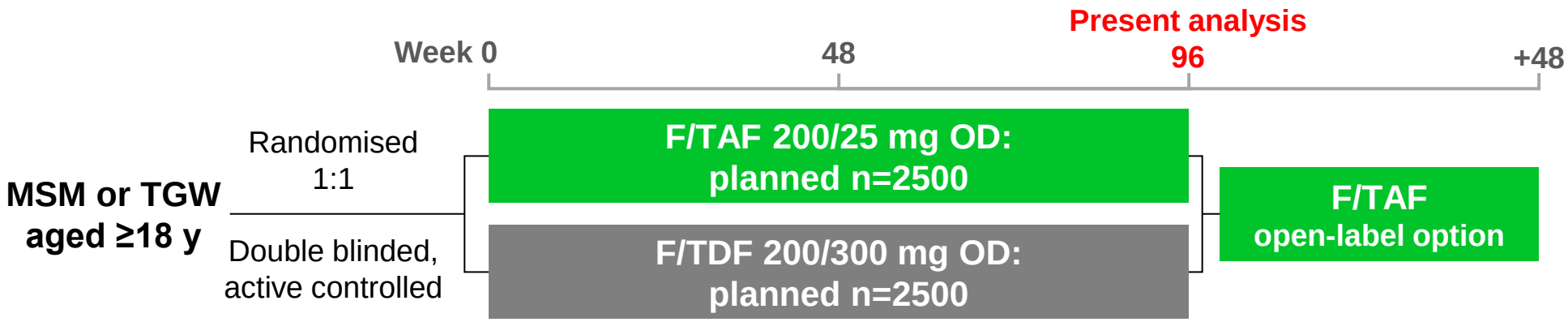
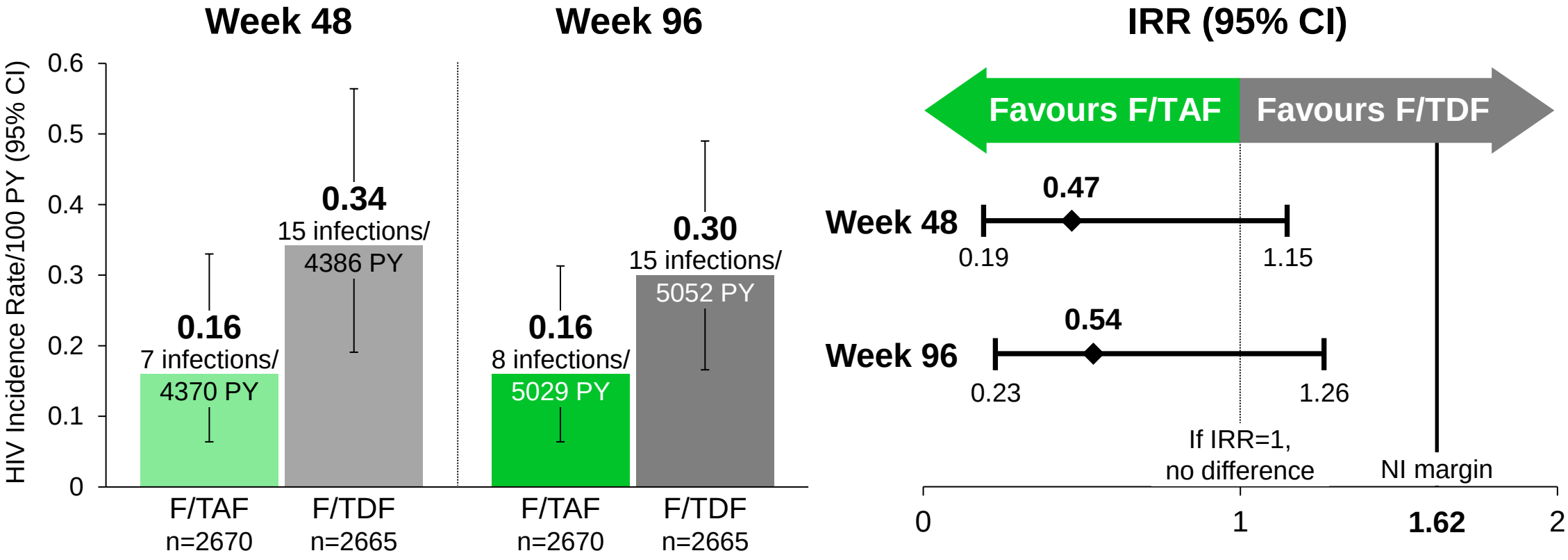
Introduction and Study Design



- The DISCOVER study (ClinicalTrials.gov NCT02842086) is an ongoing Phase 3, randomised, controlled trial evaluating the efficacy and safety of F/TAF for PrEP among cisgender men and transgender women who have sex with men (MSM, TGW) at high risk of HIV infection
- Here we present longer term results conducted after all participants completed the Week 96 visit

F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; OD, once daily; y, years

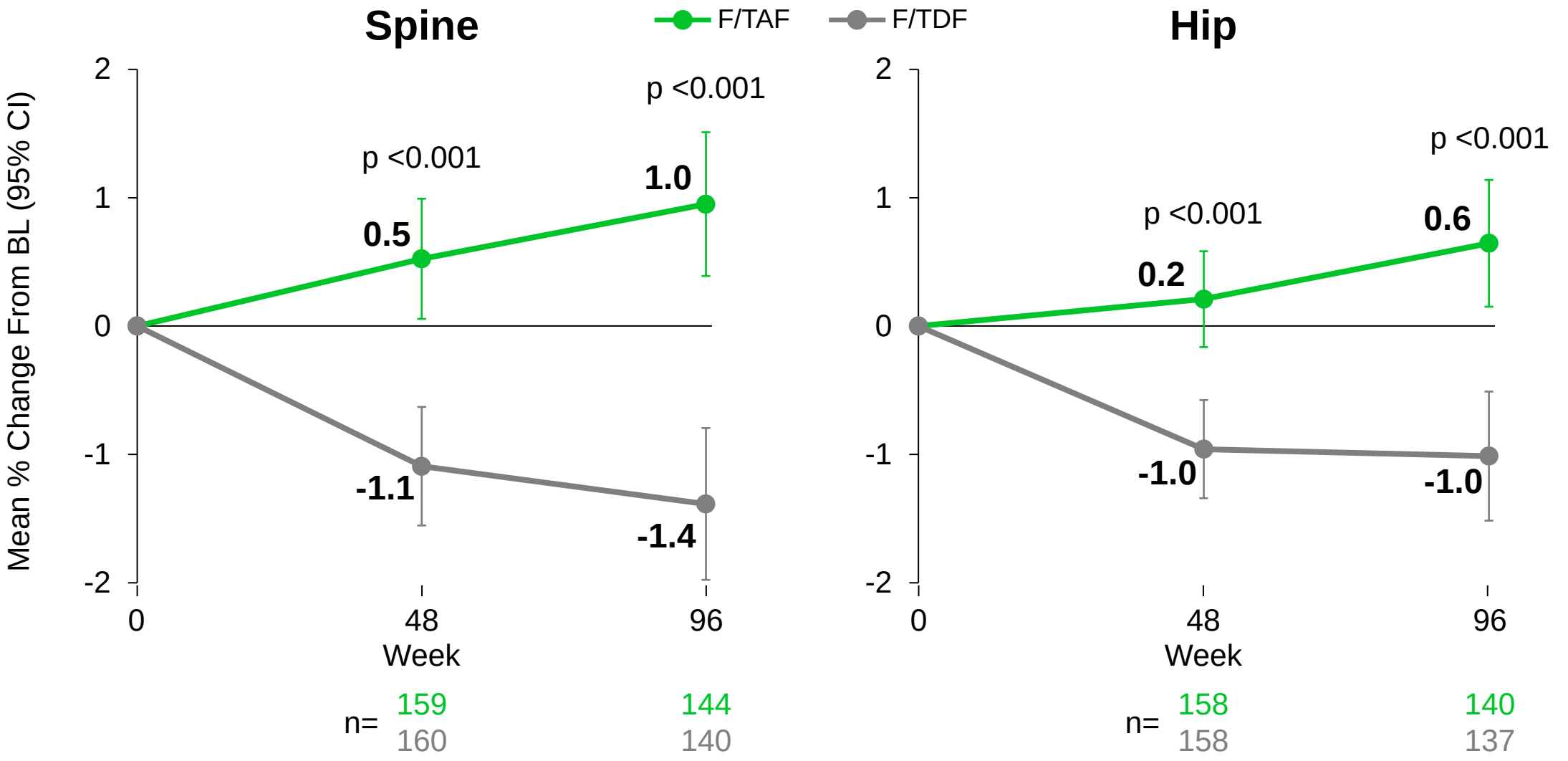
Primary Endpoint Analysis: HIV Incidence



- Primary analysis: 22 HIV infections in 8756 PY of follow-up
- Week-96 analysis: 23 HIV infections in 10,081 PY of follow-up
- F/TAF was non-inferior to F/TDF for HIV prevention as the upper bound of IRR 95% CI was <1.62

CI, confidence interval; IRR, incidence rate ratio; NI, noninferiority; PY, person-year.

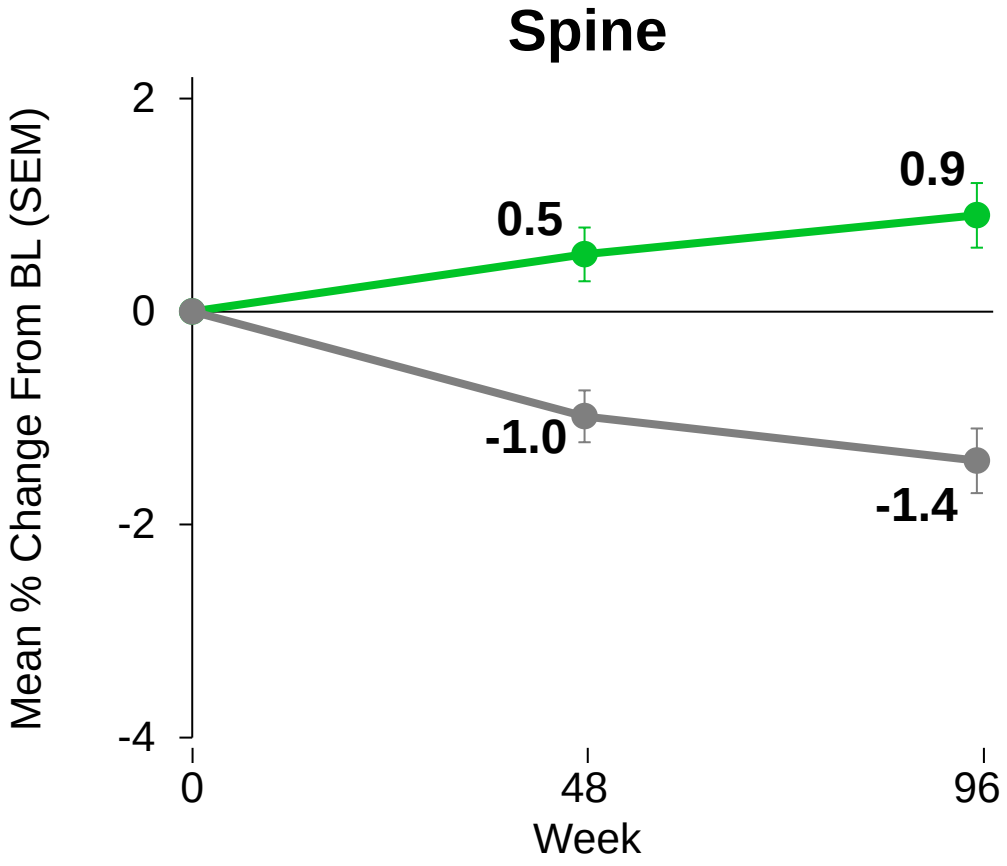
Bone Safety: BMD Substudy (n=375)*

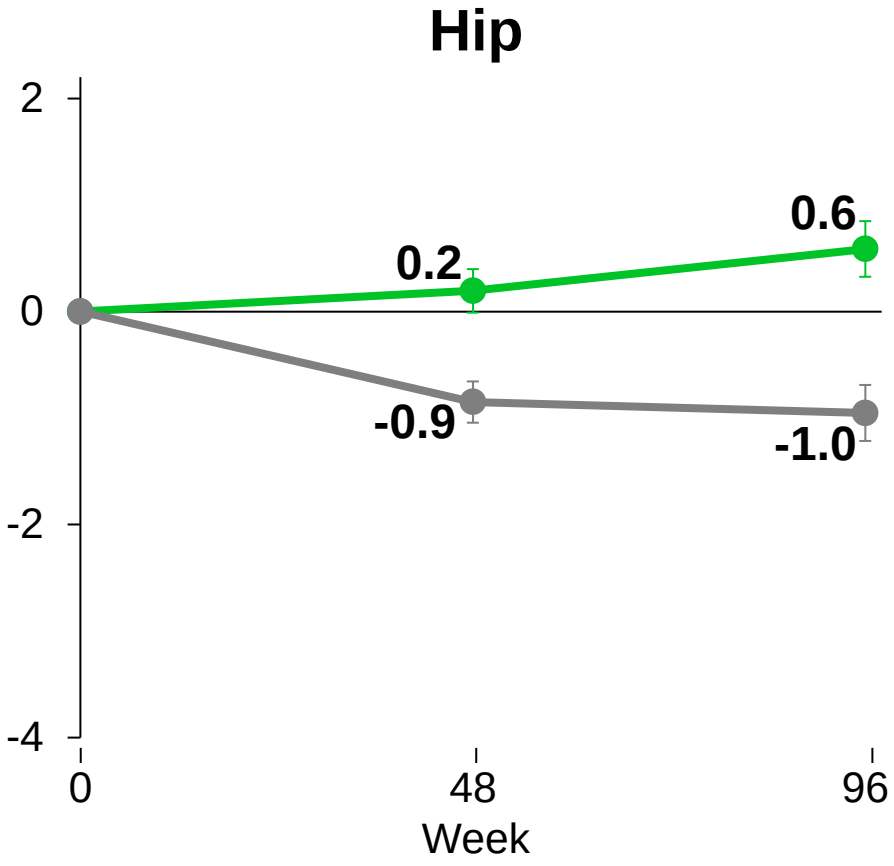


*p-values from analysis of variance model with BL F/TDF for PrEP and study arm as fixed effects. Reported fracture events: F/TAF, n=65; F/TDF, n=64.

Bone Safety: BMD Substudy (n=375)*

Aged ≥25 y





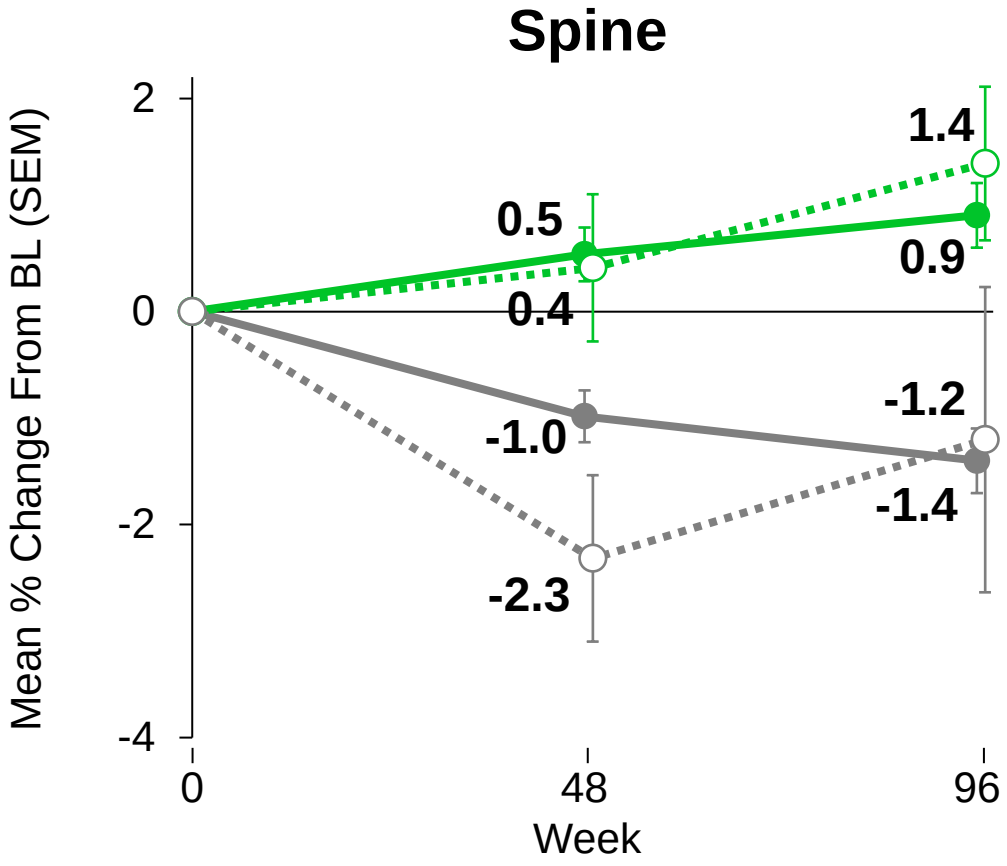
Week 96	≥25 y	
F/TAF	n=130	p <0.001*
F/TDF	n=129	

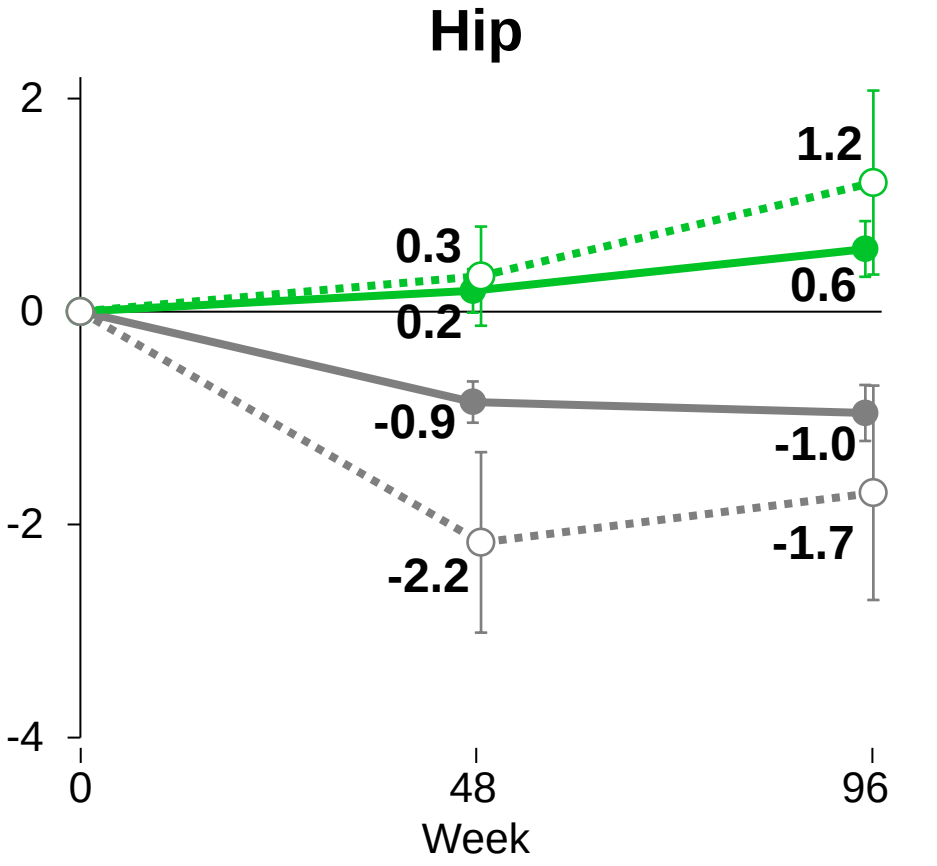
≥25 y	
n=127	p <0.001*
n=126	

*p-values from analysis of variance model with BL F/TDF for PrEP and study arm as fixed effects. SEM, standard error of mean.

Bone Safety: BMD Substudy (n=375)*

Aged ≥ and <25 y



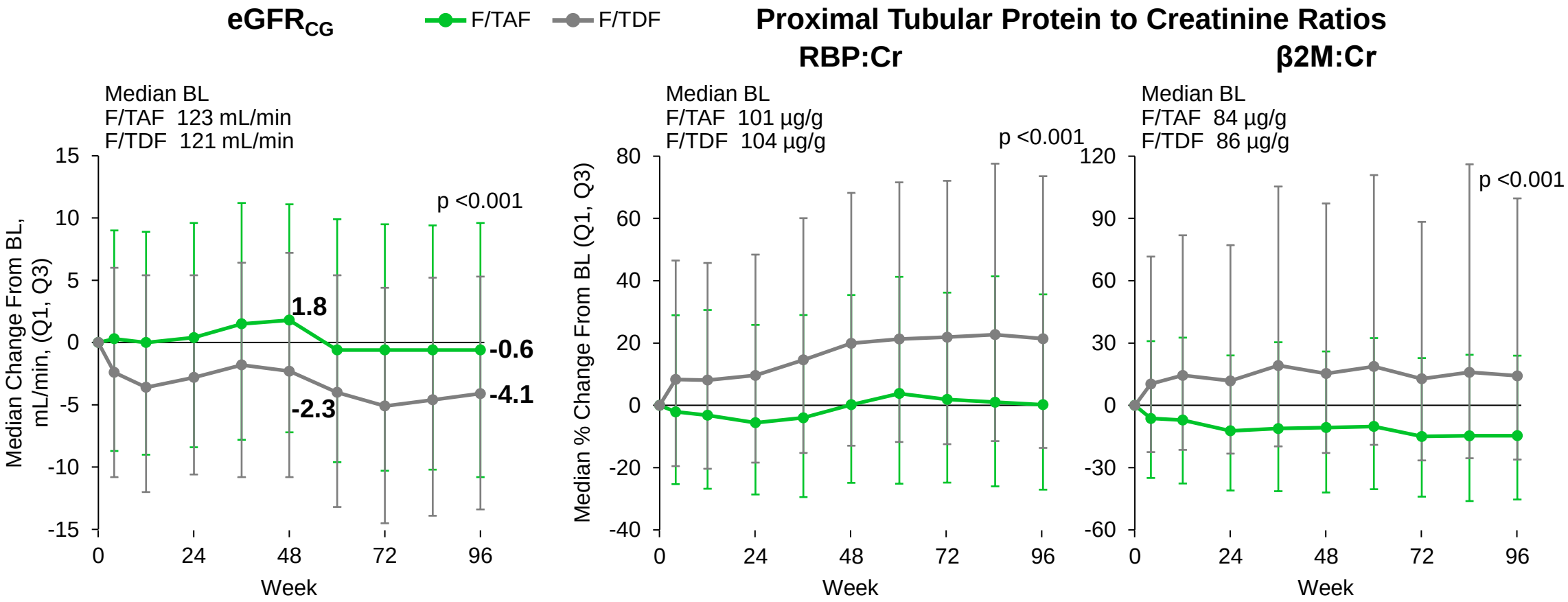


Week 96	≥25 y		<25 y	
F/TAF	n=130	p <0.001*	n=14	p=0.14*
F/TDF	n=129		n=11	

≥25 y		<25 y	
n=127	p <0.001*	n=13	p=0.035*
n=126		n=11	

*p-values from analysis of variance model with BL F/TDF for PrEP and study arm as fixed effects. SEM, standard error of mean.

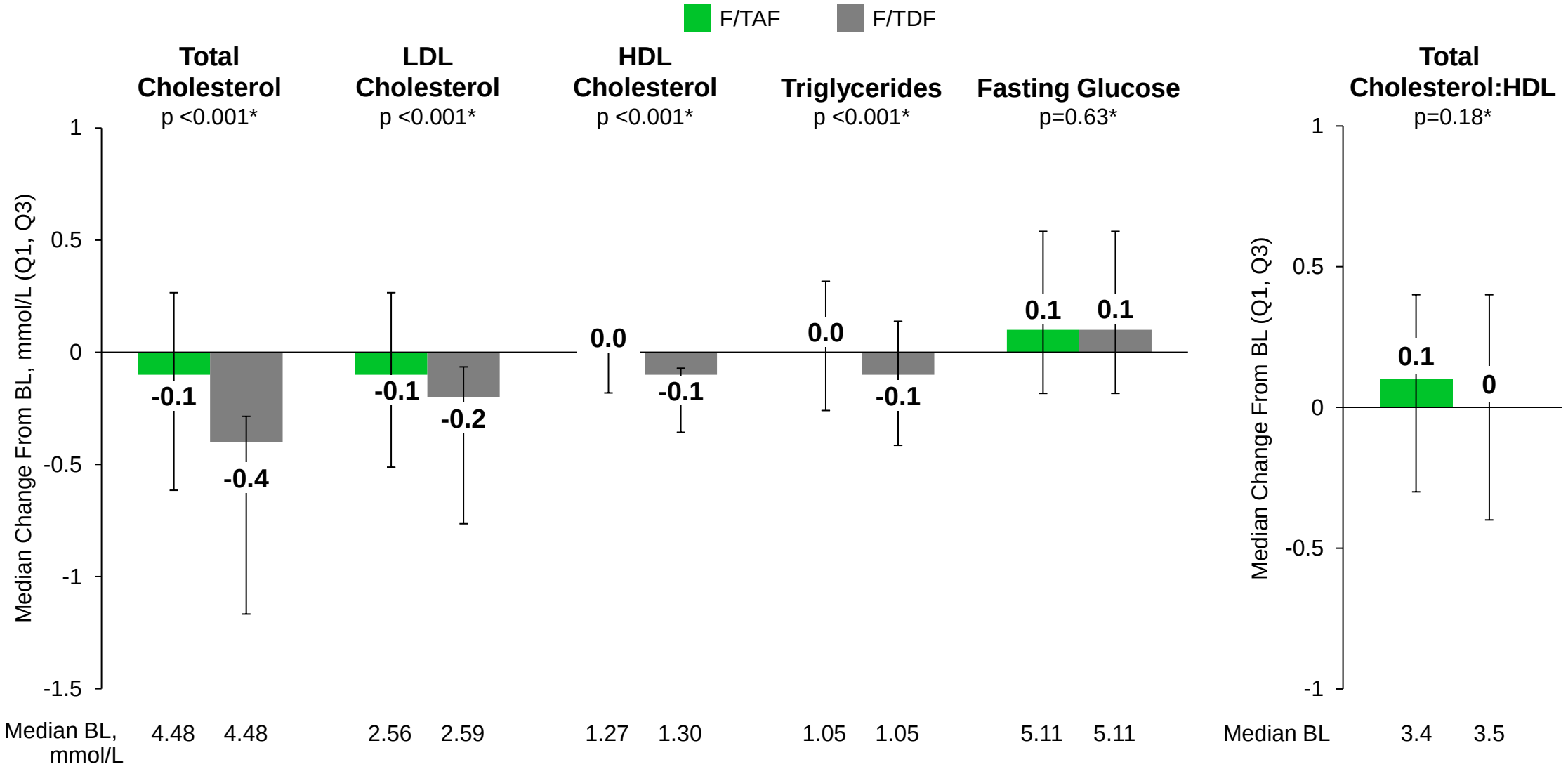
Renal Safety



- Renal discontinuations: F/TAF, n=2; F/TDF, n=6
- Fanconi syndrome: F/TAF, n=0; F/TDF, n=1

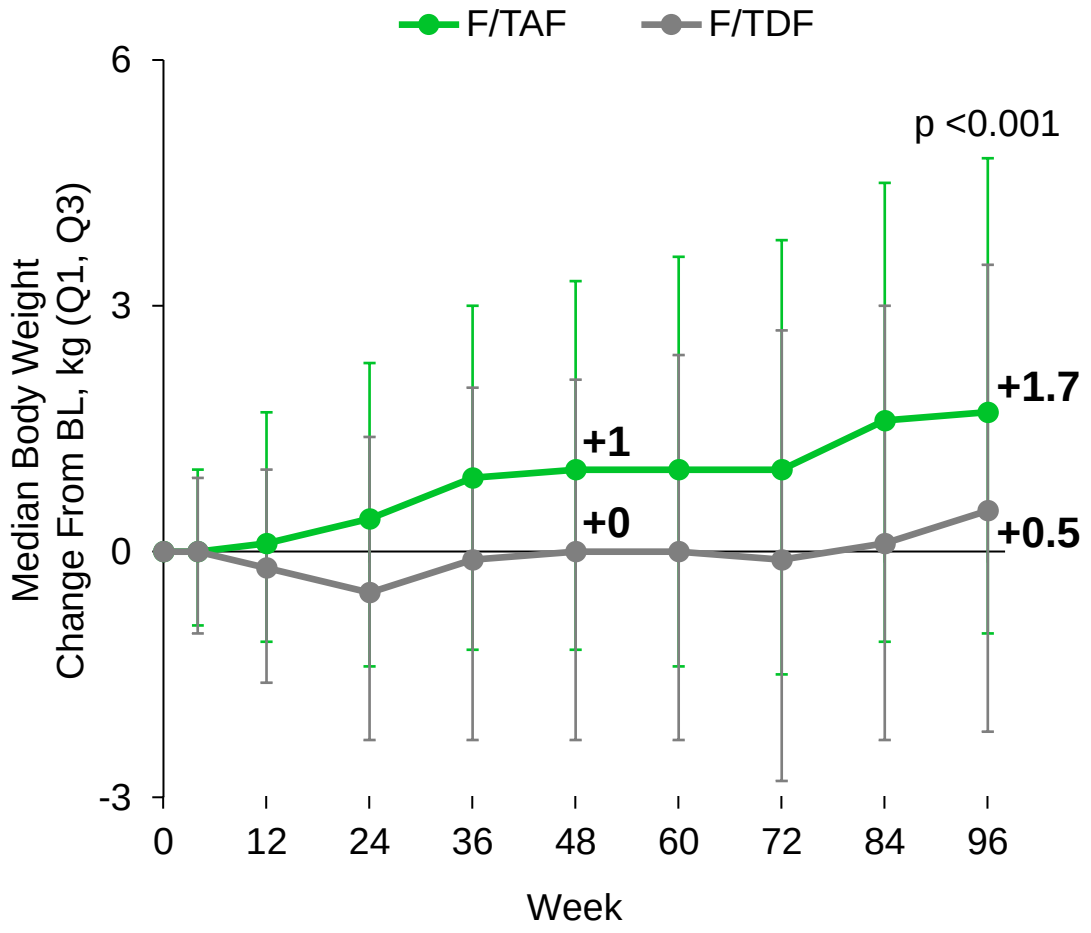
*p-values from Van Elteren test stratified by BL F/TDF for PrEP to compare 2 study arms.
β2M, β2-microglobulin; Cr, creatinine; Q, quartile; RBP, retinol-binding protein.

Fasting Lipids and Glucose at Week 96



*p-values from 2-sided Wilcoxon rank sum test to compare 2 study arms.

Body Weight



p-values for changes from baseline from analysis of covariance model including BL F/TDF for PrEP and study arm as fixed effects and BL body weight or body mass index (BMI) as a covariate.

Conclusions

- F/TAF remained non-inferior to F/TDF for HIV PrEP through 96 weeks
- DISCOVER provides the largest, single variable comparison of bone and renal safety parameters between TAF and TDF in the absence of underlying HIV or third antiretroviral agents:
  - Differences in BMD between F/TAF and F/TDF increased at week 96, with more pronounced differences in younger participants
  - Renal biomarker changes remained more favorable in participants taking F/TAF
- F/TDF was associated with greater declines in LDL and HDL, consistent with its known effects on lipids[1]. Total cholesterol:HDL ratio and fasting glucose were similar between arms."
- Weight gain was observed in both arms at 96 weeks, and was approximately 1kg greater in participants taking F/TAF. The weight gain in F/TAF arm was similar to that observed in the placebo arm of the iPrEx PrEP trial and the general population[2,3]
- F/TAF is a generally well tolerated, longer term option for PrEP

1. Tungsiripat M et al. AIDS. 2010 July 17; 24(11): 1781–1784 2. Glidden DV, et al. Clin Infect Dis 2018;67:411-9. 3. Hill JO, et al. Science 2003;299:853-5.

Acknowledgments

We extend our thanks to the participants, their families, and all participating study investigators and staff:

- **Austria:** B Haas, A Rieger;
- **Canada:** J Brunetta, JJ de Wet, J Szabo, C Tremblay, B Trottier;
- **Denmark:** J Gerstoft, G Kronborg, C Larsen, D Larsen;
- **France:** E Cua, J-M Molina, P Philibert, G Pialoux;
- **Germany:** H Jessen, G Knecht, I Krznaric, C Spinner;
- **Ireland:** C Bergin, P Mallon;
- **Italy:** A Antinori, A Lazzarin;
- **Netherlands:** M Prins;
- **Spain:** J Coll, M Crespo, J del Romero Gerrero, D Podzamczer;
- **UK:** V Apea, A Clarke, O Dosekun, R Gilson, S Kegg, C Leen, N Nwokolo, F Post, I Reeves, G Schembri, S Taylor;

USA: D Asmuth, A Avery, P Benson, M Berhe, I Brar, C Brinson, JH Burack, T Campbell, M Cespedes, M Coleman, CM Creticos, GE Crofoot, FA Cruickshank, E Daar, E DeJesus, W Dinges, S Doblecki-Lewis, T Donovan, J Flamm, JE Gallant, J Gladstein, RM Grant, R Grossberg, J Halperin, WD Hardy, CB Hare, S Hassler, R Hengel, K Henry, T Hodge, S Hosek, M Iandorio, A LaMarca, C Lucasti, S Mannheimer, CT Martorell, M Markowitz, K Mayer, A Mills, S Morris, K Mounzer, O Ogbuagu, O Osiyemi, A Petroll, J Phoenix, MN Ramgopal, B Rashbaum, GJ Richmond, PJ Ruane, L Salazar, AJ Scarsella, M Scott, P Shalit, JL Stephens, MA Thompson, G Voskuhl, BH Wade, DA Wohl, K Workowski, B Young.

This study was funded by Gilead Sciences, Inc.