Introduction

- The DISCOVER study (ClinicalTrials.gov NCT02940828) is an ongoing Phase 3, randomized, controlled trial evaluating the efficacy and safety of F/TAF for PrEP among cisgender men and transgender women who have sex with men (MSM). TDF/300 mg at high risk of HIV infection
- Interim data analysis was conducted when 100% of participants completed Week 48 and 50% completed Week 96, and demonstrated that:
  - F/TAF was noninferior to F/TDF in preventing HIV infection
  - Both drugs were well tolerated, with low rates of AE-related discontinuations
  - F/TAF had significantly better bone and renal safety outcomes vs F/TDF

Objectives

- To present longer term results conducted after all participants completed the Week 96 visit
- To present key findings to support ongoing long-term safety data

Methods

Study Design

- Eligibility: high-risk HIV
  - 2+ episodes of condomless anal sex in the past 12 wk or rectal gonorrhea/Chlamydia or syphilis in past 24 wk
  - HIV and hepatitis B virus negative, and eGFR ≥60 mL/min
  - Prior use of PrEP allowed
  - Study conducted in Europe and North America in cities/sites with high HIV incidence

Participant Disposition Through Week 96

- Total: 2,694 participants
  - F/TAF: 1,347
  - F/TDF: 1,347
  - Lost to follow-up: 225 (8.6%)
  - Participant decision: 196 (7.3%)
  - Other reasons: 29 (1.1%)
  - 53.9% remained on study drug at Week 96

Demographics and Baseline Characteristics

- Overall:
  - Median age: 32.0 years
  - Median weight: 79.6 kg
  - Median height: 169.5 cm
  - Median BMI: 25.1 kg/m²
- F/TAF:
  - Median age: 32.0 years
  - Median weight: 79.6 kg
  - Median height: 169.5 cm
  - Median BMI: 25.1 kg/m²
- F/TDF:
  - Median age: 32.0 years
  - Median weight: 79.6 kg
  - Median height: 169.5 cm
  - Median BMI: 25.1 kg/m²

Results

Primary Endpoint Analysis: HIV Incidence

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

Categorical BMD Changes (By Percent Change) at Week 96

- Week 96:
  - Spine: +1.7%
  - Hip: -1.0%

Overall Safety Summary

- F/TAF vs F/TDF
- Any AE (%): 93 vs 93
- Drug-related AE (%): 21 vs 24
- Grade ≥3 AE: 49 vs 47
- Serious AE: 7 vs 6
- AE leading to discontinuation (%): 1 vs 2

Renal Safety

- BL eGFR 60–200 mL/min
- Median % Change From BL (Q1, Q3)
- F/TAF: 101 µg/g
- F/TDF: 114 µg/g

Conclusions

- F/TAF remained noninferior 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; BMD declines of ≥3% were more common in participants taking F/TDF, with more pronounced differences in younger participants
- Renal biomarker changes remained more favorable in participants taking F/TAF, including in older participants and those with reduced eGFR
- F/TDF was associated with greater declines in both LDL and HDL but total cholesterol: HDL ratios or fasting glucose remained similar across both study arms at 96 weeks
- 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 iPrEx PrEP trial and the general population

References & Acknowledgments

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Disclosures

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