Changes in renal laboratory markers and bone mineral density in treatment-naive HIV-1-infected adolescents initiating INSTI-based single-tablet regimens containing tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF)

**Methods**
- Cross-study comparison of 2 ongoing open-label, single-arm studies in treatment-naive adolescents
  - Study 292-0106: E/C/F/TAF administered for 48 weeks (N=50)
  - Study 236-0112: E/C/F/TDF administered for 48 weeks (N=50)
- Primary endpoint: safety
- Secondary endpoint: viral suppression
- For both studies key inclusion/exclusion criteria:
  - Age ≥12 to < 18 years
  - Weight >35 kg
  - HIV-1 RNA >1000 copies/mL
  - No prior ARV therapy
  - CD4 count >100 cells/mm³

**Study Assessments and Analysis Methods**
- Safety assessments
  - Adverse events and laboratory assessments: hematology, chemistry, renal, and bone mineral density in treatment-naive adolescents initiating INSTI-based single-tablet regimens containing tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF)
- Efficacy assessments
  - Dual X-ray absorptiometry (DXA) of spine and total body less head (TBLH) at baseline and every 24 weeks
- Statistical methods
  - Cross-calibration between DXA scanner types (Hologic and Lunar)
  - Calculation of standard and height-adjusted Z-scores and predicted BMD change
- SNP analysis algorithm for HIV-1 RNA < 50 copies/mL at Week 24

**Background: E/C/F/TAF and E/C/F/TDF**
- E/C/F/TDF (commercially available as Stribild) and E/C/F/TAF (not commercially available yet) are single pill formulations that both contain elvitegravir (EVG) 150 mg, cobicistat (COBI) 150 mg, and emtricitabine (FTC) 200 mg
  - E/C/F/TAF contains TAF 10 mg
  - E/C/F/TDF (Stribild) contains TDF 300 mg
- Two phase 3 double blind adult studies¹ comparing E/C/F/TAF to E/C/F/TDF demonstrated:
  - Noninferior efficacy of E/C/F/TAF
  - Significantly reduced renal and bone effects with E/C/F/TAF
- Two single-arm open-label studies² of E/C/F/TAF and E/C/F/TDF conducted in treatment-naive adolescents have shown:
  - These STRs are well tolerated
  - Plasma levels of all components are similar to those in adults

**Disclosure of Interest Statement:**
- Study 106 and 112 are Gilead Sciences sponsored Phase II studies
- Dr. Prasitsuebsai has received funding from, acted as an advisor for, and/or participated in clinical research for: Gilead Sciences, Janssen, Merck, Bristol Myers Squibb

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1. Lee W et. al. Lancet 2015;385:2606
2. Pharm 2013;10:459
Most failures were associated with decreased adherence

Most AEs mild or moderate and unrelated to study treatment

No deaths or adverse events (AEs) leading to treatment discontinuation

No cases of proximal renal tubulopathy or Fanconi syndrome

Serious adverse events:

- Urinary retention, neuropathy, pain, constipation
- Conduct disorder, polysubstance abuse, bipolar disorder
- Intermediate uveitis, visual disorder

No emergent resistance

All subjects achieved HIV

- All subjects achieved HIV-1 RNA < 50 copies/mL by Week 12
- Proportion with HIV-1 RNA < 50 copies/mL at Week 24: E/C/F/TAF 90% (45/50), E/C/F/TDF 88% (44/50)
- Most failures were associated with decreased adherence
- No emergent resistance

Creatinine and Cystatin C by Visit

- Median change in Cr (mg/dL) at Week 24: E/C/F/TAF +0.08, E/C/F/TDF +0.08
- Median change in GFR (mL/min/1.73 m²) at Week 24: E/C/F/TAF -15.0, E/C/F/TDF -14.0
- Slight decrease in Cystatin C (not affected by COBI) in both groups
Both groups exhibited rapid virologic response and high rates of virologic success at Week 24, with no emergent resistance observed in either group. The E/C/F/TAF group had increased median spine BMD at Week 24 (+1.3%) compared with a decrease (-1.0%) in E/C/F/TDF group. These data support use of both regimens in treatment-naive adolescents and suggest potential renal and bone safety advantages of TAF.

Conclusions

While being cognizant that this was a cross-study comparison and there were differences (age, gender, geography, mode of transmission) at baseline, we observed:

- Both groups exhibited rapid virologic response and high rates of virologic success at Week 24, with no emergent resistance.
- E/C/F/TAF and E/C/F/TDF generally well tolerated.
- Small observed increases in serum Cr, consistent with known effect of cobicistat in adults.
- E/C/F/TAF decreased renal biomarkers, similar to that observed in adult E/C/F/TAF phase 3 studies.
- E/C/F/TAF group had increased median spine BMD at Week 24 (+1.3%) compared with a decrease (-1.0%) in E/C/F/TDF group.

Changes in Spine Bone Mineral Density

- At Week 24, compared to spine BMD at baseline a decrease of ≥4% was seen in:
  - 47% participants (5.7%) in the E/C/F/TAF cohort
  - 56% participants (21%) in the E/C/F/TDF cohort.

Changes in Renal Tubular Biomarkers Through Week 24

- $\beta_2$-microglobulin
- Retinol Binding Protein (RBP)
- Protein (UPCR)

Changes in Spine Bone Mineral Density

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Our patients and their families