Effect of Age on Efficacy and Safety of Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide (E/C/F/TAF) in Virologically-Suppressed, HIV-1-Infected Participants Aged ≥65 Years: A Pooled Analysis of Two Phase 3 Trials

Poster P146

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Background

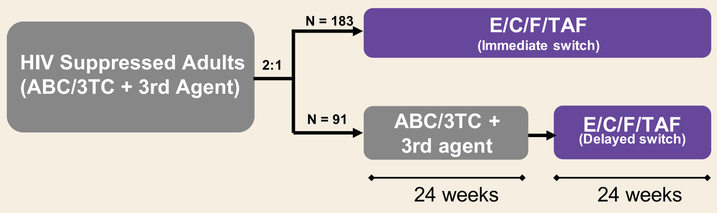
- As the HIV population ages, analyzing safety and efficacy data for antiretroviral (ARV) agents in older adults living with HIV is increasingly important.
- The population of people living with HIV infection continues to age (median age approaches 50 years in many locations).
- Older individuals may be on more concomitant medications and ensuring the safety of ART in this population is critical.
- TAF is a tenofovir prodrug associated with 90% lower tenofovir plasma levels resulting in greater renal and bone safety than tenofovir disoproxil fumarate (TDF).
- We evaluated the efficacy and safety of E/C/F/TAF in individuals less than and greater than or equal to 65 years of age.

Methods

- In two international, multicenter, Phase 3 trials, ARV-experienced participants with HIV RNA < 50 copies/mL were randomized 2:1 to receive:
  - 1) E/C/F/TAF for 48 weeks or continued current abacavir/lamivudine (ABC/3TC)-based regimen for 24 weeks followed by a delayed switch to E/C/F/TAF for another 24 weeks (292-1823) or
  - 2) E/C/F/TAF or continued TDF-based regimen for 48 weeks (292-1826, all subjects were ≥60 years).
- This pooled analysis of the E/C/F/TAF arms evaluated efficacy (HIV-1 RNA <50 copies/mL, FDA snapshot analysis) and safety through Week 48 for participants categorized by age (< and ≥65 years).
- Randomization was not stratified by age in study 1826.

Switch from ABC to E/C/F/TAF
GS-US-292-1823

Multicenter, randomized, open-label study



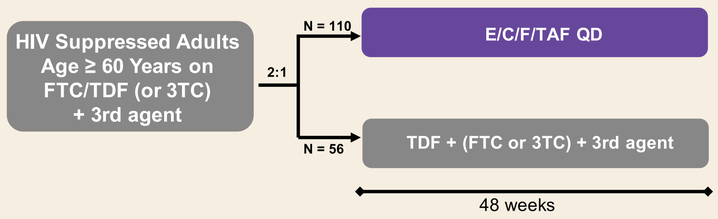
- **Eligibility criteria**
  - HIV-1 RNA <50 c/mL for ≥6 months

Stratified by age < or ≥ 60 years

- **Primary Endpoint**
  - HIV-1 RNA < 50 copies/mL at Week 24 (FDA snapshot analysis)
- **Secondary Endpoints**
  - HIV-1 RNA < 50 copies/mL at Weeks 12 and 48 (FDA snapshot analysis)
  - CD4 change at week 24

Switch from TDF to E/C/F/TAF for Age ≥ 60
GS-US-292-1826

Multicenter, randomized, open-label, active control, 48-week study



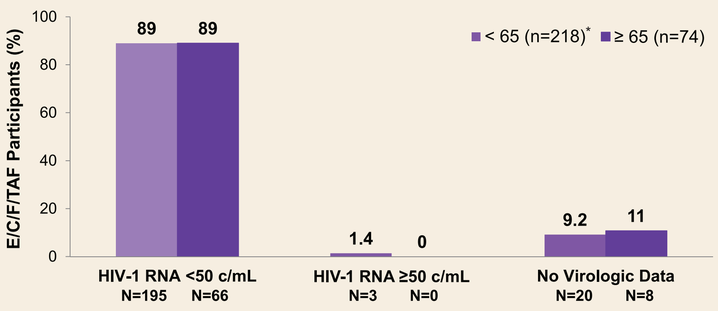
- **Eligibility criteria**
  - HIV-1 RNA <50 c/mL for ≥6 months
- **Primary Endpoint**
  - Mean percent change from Day 1 to Week 48 in spine and hip BMD by DXA
- **Secondary Endpoints**
  - Mean percent change from Day 1 to Week 24 in spine and hip BMD by DXA
  - Safety profile: adverse events, clinical laboratory tests
  - HIV RNA < 50 copies/mL at Week 24 and 48 using FDA snapshot

Results

Baseline Characteristics

	E/C/F/TAF Age <65 N=219	E/C/F/TAF Age ≥65 N=74
Median age, years (range)	51 (25-64)	69 (65-80)
Female, n (%)	27 (12)	14 (19)
Race, n (%)		
White	187 (85)	66 (89)
Black or African descent	25 (11)	4 (5)
Median estimated GFR_{CG}, mL/min (range)	98 (51-212)	74 (28-125)
Mode of Infection		
MSM	133 (61%)	32 (43%)
Heterosexual	79 (36%)	33 (45%)
Median BMI, (range)	24.9 (17.7-50.4)	25.7 (17.2-37.2)
HIV RNA < 50 copies/mL at baseline	213 (97)	73 (99)
Median CD4 count, cells/mm^3	651 (183-1818)	608 (121-1286)
Baseline Regimen		
NNRTI	127 (58%)	48 (65%)
INSTI	55 (25%)	18 (24%)
PI	37 (17%)	8 (11%)
NRTI backbone was FTC/TDF	57 (26%)	52 (70%)
Medical History of Diabetes		
Diabetes	15 (7%)	13 (18%)
Hypertension	49 (22%)	41 (55%)
Hyperlipidemia	66 (30%)	25 (34%)
Cardiovascular Disease	8 (4%)	2 (3%)

E/C/F/TAF Virologic Outcomes at Week 48 By Age



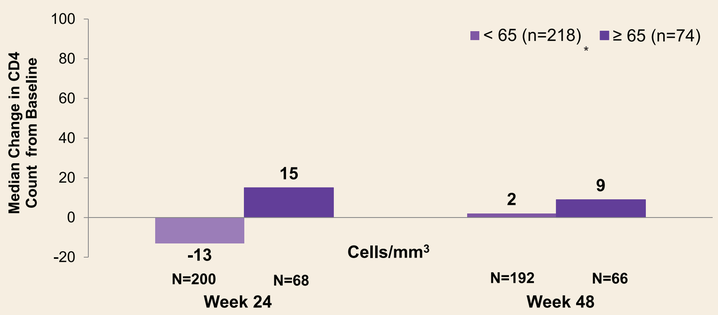
* One subject enrolled in the 292-1826 was excluded due to receiving a regimen that did not include TDF

Virologic Outcomes at Week 48

	E/C/F/TAF Age <65 (n=219)	E/C/F/TAF Age ≥65 (n=74)
HIV-1 RNA < 50 c/mL	89% (195)	89% (66)
HIV-1 RNA ≥ 50 c/mL	1.4% (3)	0
HIV-1 RNA ≥ 50 c/mL in W48 Window	0.5% (1)	0
DC Study Drug Due to Lack of Efficacy	0	0
DC Study Drug Due to AE/Death and Last Available HIV-1 RNA ≥ 50 c/mL	0	0
DC Study Drug Due to Other Reasons and Last Available HIV-1 RNA ≥ 50 c/mL	0.9% (2)	0
No Virologic Data in W48 Window	9% (20)	11% (8)
DC Study Drug Due to AE/Death and Last Available HIV-1 RNA < 50 c/mL	3% (7)	7% (5)
DC Study Drug Due to Other Reasons and Last Available HIV-1 RNA < 50 c/mL	4% (8)	3% (2)
Missing Data During Window but on Study Drug	2% (5)	1% (1)

c/mL, copies/mL; DC, discontinued

Median Change in CD4 Count from Baseline through Week 48



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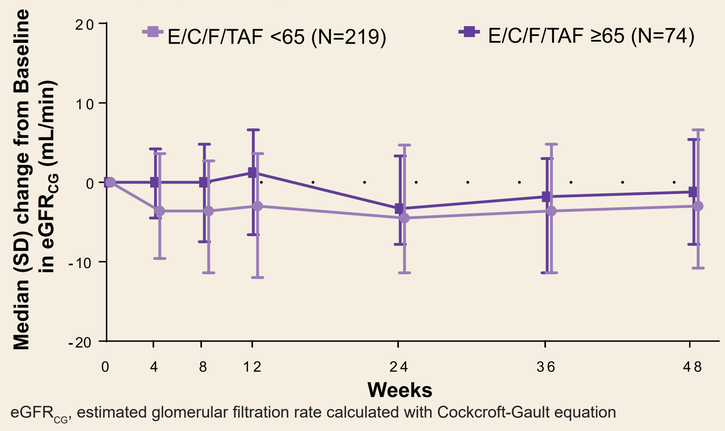
Treatment-Emergent Adverse Events through Week 48 By Age

	E/C/F/TAF Age <65 (n=219)	E/C/F/TAF Age ≥65 (n=74)
Any Grades 2, 3 and 4 Study Drug-Related AE	6.4% (14)	5.4% (4)
Any Grades 3-4 Study Drug-Related AEs	0.5% (1)	1.4% (1)
Grades 3 or 4 Lab AEs	17% (37)	9.5% (7)
Any Study Drug-Related Serious AE	0	0
AEs Leading to Study Drug Discontinuation	3.7% (8)	5.4% (4)*
Renal AEs Leading to Study Drug Discontinuation	0	0
Treatment-Emergent Fractures	0.5% (1)	1.4% (1)
Death	0	1.4% (1)**

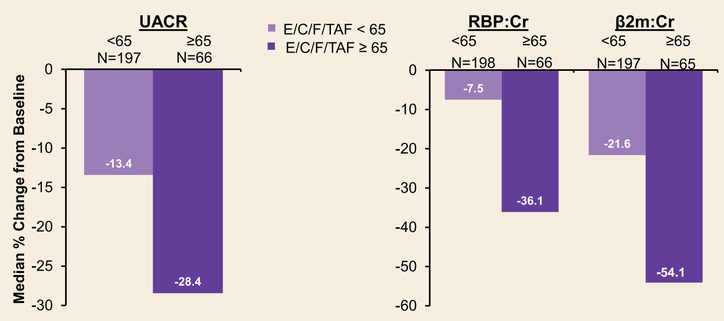
*for age >= 65 group: 1) constipation, arthralgia, myalgia; 2) diarrhea; 3) flatulence; 4) hepatocellular injury; **68 yo White male with history of DM1, dyslipidemia, TIAs and history of Aspergillus lung abscess. Hospitalized for 24 days and expired Feb 25, 2018 due to superinfection of lung abscess. Death was not treatment-related and occurred off-study

Estimated Glomerular Filtration Rate: Median Changes from Baseline by Age through Week 48



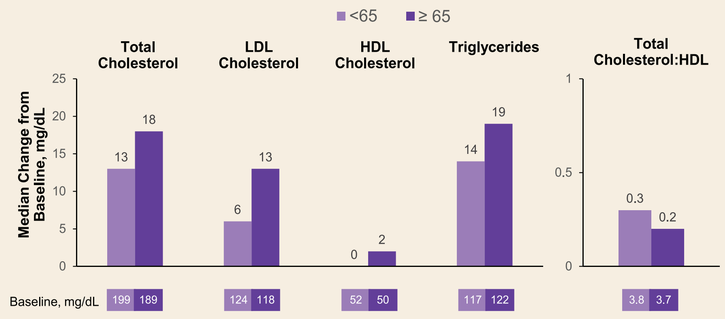
$eGFR_{CG}$, estimated glomerular filtration rate calculated with Cockcroft-Gault equation

Renal Biomarker Changes (%) at Week 48 By Age



*Complete renal biomarker panel was collected up to Week 48
UACR, urine albumin/creatinine; RBP:Cr, retinol-binding protein/creatinine; β2m:Cr, urine beta-2-microglobulin/creatinine

Changes in Fasting Lipids at Week 48



- There were no clinically significant changes in fasting lipids 48 weeks after switching to E/C/F/TAF
- Similar proportions of participants were on lipid-modifying medication
  - At baseline: < 65 year old 26%; ≥ 65 year old 34%
  - Initiated during study: < 65 year old 3.2%; ≥ 65 year old 0%

Conclusions

- Through W48, rates of virologic suppression were high and similar between participants < 65 and ≥ 65 years.
- Adverse events, adverse events leading to discontinuation, and tolerability were comparable between groups.
- Concentrations of 3 renal biomarkers decreased more in those ≥ 65 years than in younger participants.
- The W48 efficacy and safety data support the switch to E/C/F/TAF in HIV-infected, treatment experienced, HIV-1 RNA suppressed people ≥ 65 years old.

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