The Safety and Efficacy of E/C/F/TDF in Treatment-naïve Women with HIV-1 Infection (WAVES Study): Week 96 Results

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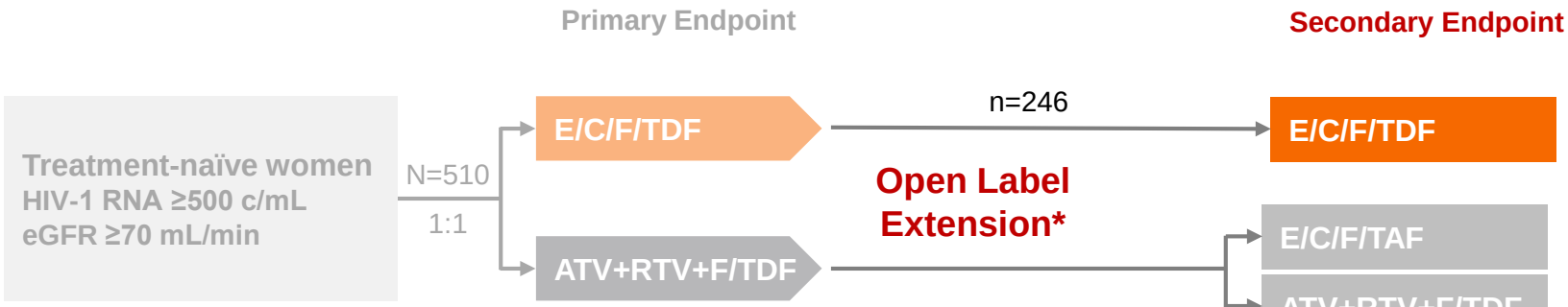
Background

- Worldwide, women comprise 51% of people living with HIV but remain underrepresented in clinical trials
- The integrase inhibitor-containing single tablet regimen of elvitegravir, cobicistat, emtricitabine, and tenofovir disoproxil fumarate (E/C/F/TDF) demonstrated superior efficacy when compared to a protease inhibitor regimen of atazanavir boosted by ritonavir (ATV+RTV) plus F/TDF in 575 treatment-naïve women at Week 48[1]
- Virologically suppressed women receiving E/C/F/TDF were given the option to enter an open-label extension (OLE) phase, in which they could continue E/C/F/TDF

1. Squires et al. Lancet HIV 2016; 3: e410–20.

Methods: Study Design

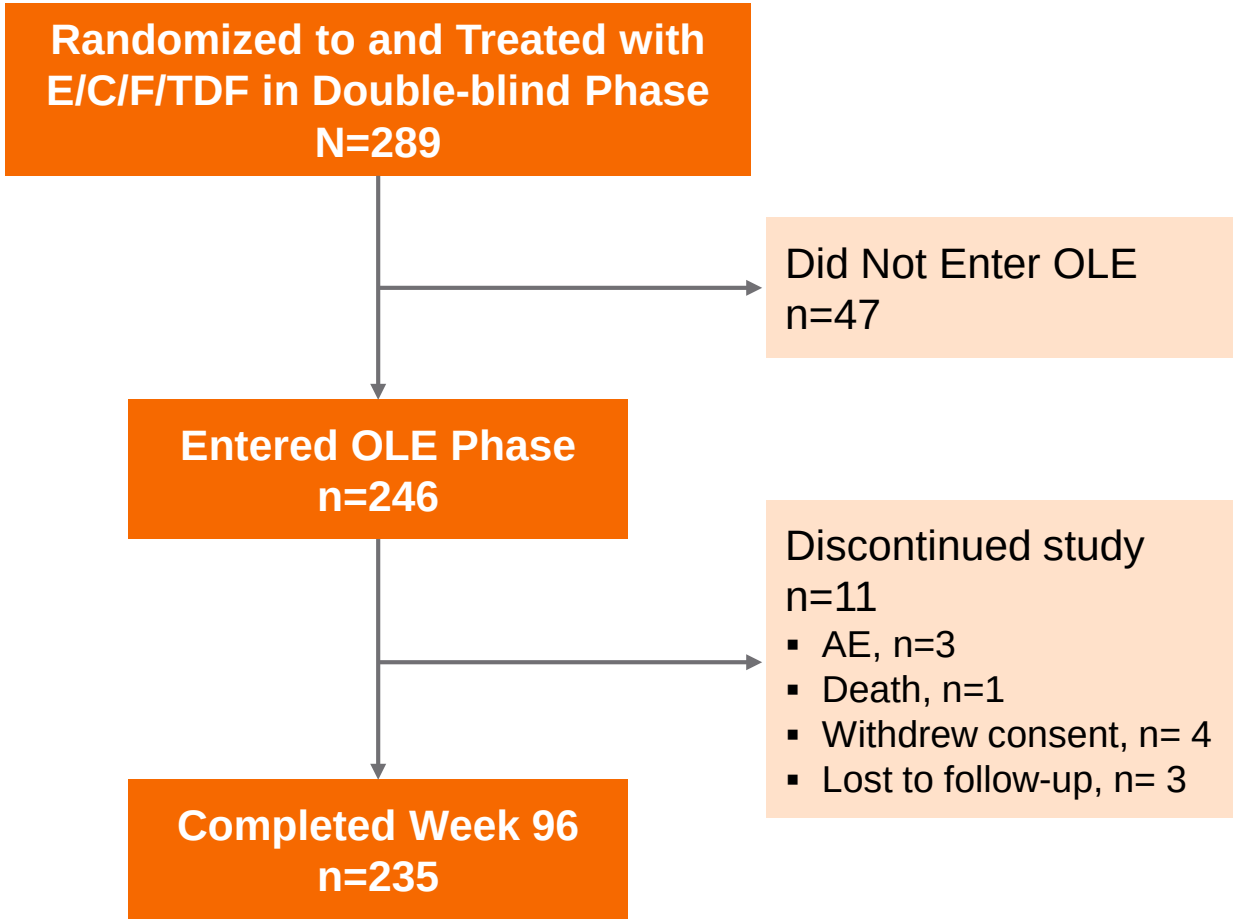


*Key criteria for enrollment to the open label extension: VL<50 c/mL and eGFR≥50

- Phase 3b, randomized, double-blind, active-controlled phase with randomized, open-label, active-controlled extension phase (NCT01705574)
- Primary efficacy endpoint in randomized phase met: proportion of participants with HIV-1 RNA <50 c/mL based on Week 48 FDA snapshot analysis[1]
- Secondary endpoints: efficacy, safety, and tolerability at Week 96 in OLE
- OLE Week 96 analysis (E/C/F/TDF) is presented

1. Squires et al. Lancet HIV 2016; 3: e410–20.

Results:
Disposition for Open-label Extension Phase



Results: Baseline Characteristics

		E/C/F/TDF n=289
Median age, y (Q1, Q3)		34 (28, 43)
Race, %	White	44
	Black	49
	Asian	3
Heterosexual mode of infection, %		96
HIV disease, %	Asymptomatic	81
	AIDS	4
Mean BMI, kg/m^2 (SD)		26 (7)
Positive HBsAg, %		3
Positive HCV antibody, %		8
Median HIV-1 RNA, log_{10} copies/mL (Q1, Q3)		4.46 (4.09, 4.97)
Patients with HIV-1 RNA log_{10} copies/mL, %	≤100,000	76
	>100,000–400,000	15
	>400,000	9
Median CD4 cell count, cells/mm^3 (Q1, Q3)		344 (246, 466)
Patients with <200 cells/mm^3, %		17

BMI, body mass index; HBsAG, hepatitis B surface antigen; HCV, hepatitis C virus; Q, quartile; SD, standard deviation.

Results: Virologic Outcome at Week 96

- 85% (235/278) maintained HIV-1 viral load <50 copies/mL at Week 96
- In 7% (19/278), virologic data not available
  - 7 patients discontinued due to adverse events (AEs) or death
  - 12 discontinued for other reasons (lost to follow-up, noncompliance, protocol violation) and last available HIV-1 RNA <50 copies/mL
- 9% (24/278) virologic failure
  - 6 had HIV-1 RNA ≥50 copies/mL
  - 15 discontinued for other reasons (lost to follow-up, noncompliance, protocol violation) and last available HIV-1 RNA ≥50 copies/mL
  - 3 took additional antiretroviral medications
- No participant had emergent resistance to study drug

Results: Study Drug Related Adverse Events*

AE, %	E/C/F/TDF N=289
Any AEs	**30**
Nausea	11
Headache	4
Vomiting	4
Decreased appetite	3
Diarrhea	3
Dizziness	3

*AE in >2% of patients.

Results: Adverse Events Leading to Study Drug Discontinuation

AE, %	E/C/F/TDF N=289
Discontinuation due to AE*	**3**
Pulmonary tuberculosis	1
Rash	1
Dyspepsia	<1
Nausea	<1
Jaundice	<1
Alanine aminotransferase increased	<1
Pruritus	<1

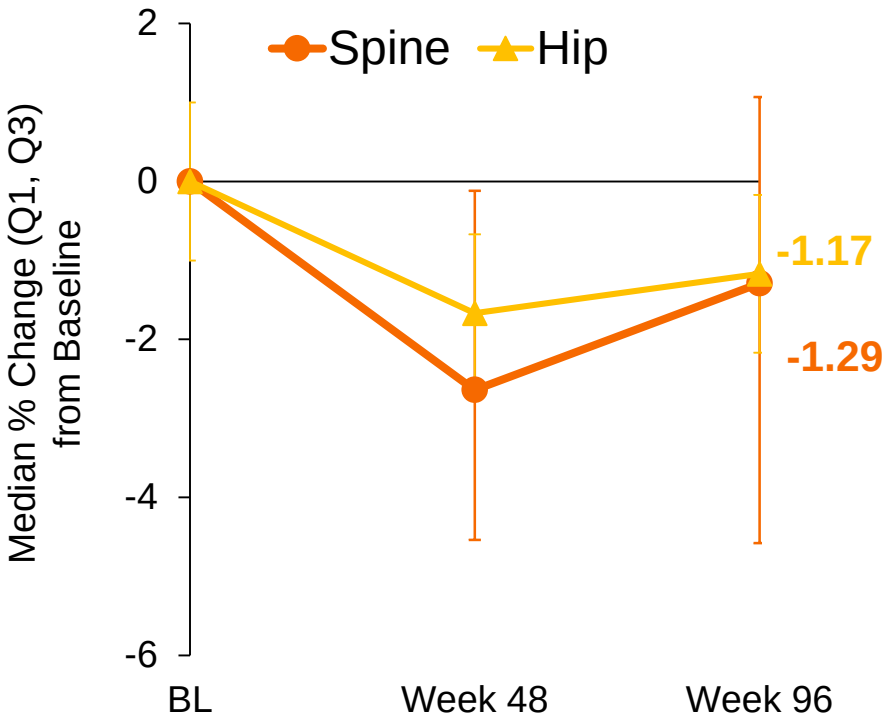
*Some patients had >1 AE leading to discontinuation.

Results: Grade 3 or 4 Lab Abnormalities

AE, %	E/C/F/TDF N=289
Any grade 3 or 4 lab abnormality	**31**
Urine RBC (hematuria, quantitative)	17
LDL (fasting)	4
Neutrophils	3
Amylase	2
AST	2

*Abnormalities in >2% of patients.
AST, aspartate aminotransferase.

Results:
Changes in Spine and Hip BMD Through Week 96



n=	138	128	106
n=	136	126	105

Results: Pregnancies

	E/C/F/TDF n=289
Pregnancies, n	24*
Live births	10†
Elective abortions	7
Spontaneous abortions	3
Ectopic pregnancy	1
Ongoing pregnancy	1
No reported outcomes	2

*3 women each had 2 pregnancies, 20 of these 21 women remained on E/C/F/TDF;
†1 woman had 2 live births.

- No birth defects were reported, and no study-drug related AE were reported during pregnancies

Conclusions

- E/C/F/TDF demonstrated durable efficacy with no emergent resistance development through 96 weeks
- 7% of the women became pregnant while on E/C/F/TDF, and all except one remained on study drug
- E/C/F/TDF continued to be a safe and well tolerated treatment in ART-naive, HIV-infected women

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