ARV Therapies and Therapeutic Strategies

REPORTING ON EACS 2015

Comprehensive Expert Review and Discussion of Key Presentations

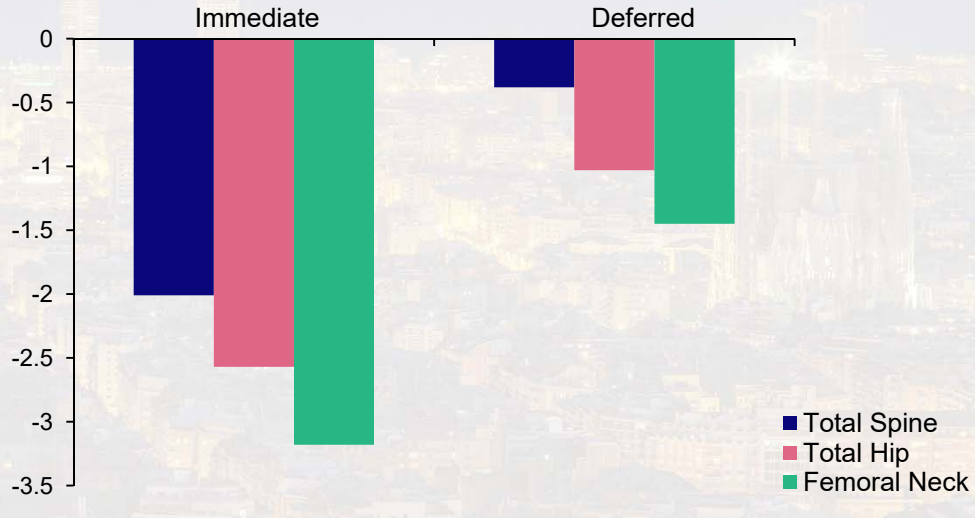
An Independent CME Activity Jointly Provided by Postgraduate Institute for Medicine and ViralEd, Inc.
The coverage is not sanctioned by the conference organizers and is not an official part of the conference proceedings.

Effects of Immediate Versus Deferred Initiation of Antiretroviral Therapy on Bone Mineral Density: A Substudy of the INSIGHT Strategic Timing of Antiretroviral Therapy (START) Study

Jennifer Hoy (Australia)

Abstract ADRLH-62

START: % BMD change through follow-up



Hoy J, et al; 15th EACS, Barcelona, Spain, October 21-24, 2015; Abst. ADRLH-62.

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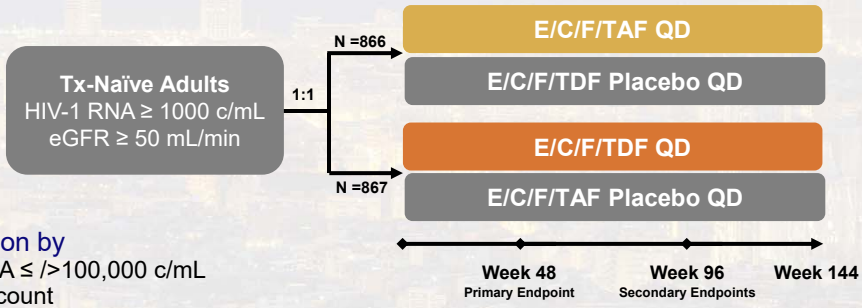
A Randomized, Double-Blind Comparison of Tenofovir Alafenamide (TAF) vs. Tenofovir Disoproxil Fumarate (TDF), Each Coformulated with Elvitegravir, Cobicistat and Emtricitabine (E/C/F) for Initial HIV-1 Treatment: Week 96 Results

D. Wohl, S. Oka, N. Clumeck, A. Clarke, C. Brinson, K. Tashima, J. Stephens, J. Arribas, B. Rashbaum, A. Chéret, J. Brunetta, C. Mussini, P. Tebas, P. Sax, L. Zhong, M. Das, M. Fordyce

Abstract LBBPD1/1

Studies 104 and 111: ART-Naïve Adults, Week 96 Combined Analysis Study Design

Two Phase 3, International, randomized, double-blind, active-controlled studies



- Stratification by
  - HIV-1 RNA ≤ />100,000 c/mL
  - CD4 cell count
  - Geographic region
- Primary Endpoint
  - Non-inferiority (12% margin) of E/C/F/TAF to E/C/F/TDF based on HIV-1 RNA <50 copies/mL* at Week 48 by FDA Snapshot analysis†
- Secondary Endpoints
  - Efficacy, safety** and tolerability observed through Week 96, Week 144

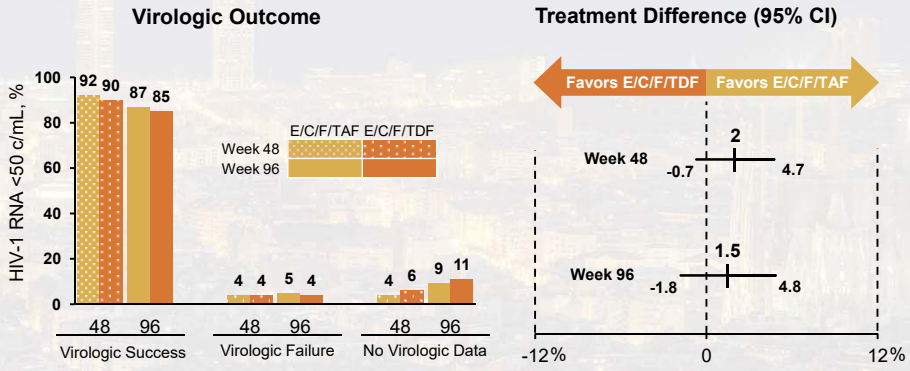
* Wohl D, et al. CROI 2015. Seattle, WA. Oral #113LB
** Sax P, et al. CROI 2015. Seattle, WA. Oral #143LB
Wohl D, et al; 15th EACS, Barcelona, Spain, October 21-24, 2015; Abst. LBBPD1/1. ClinicalTrials.gov Identifier: NCT01780506 and NCT01797445

Studies 104 and 111: ART-Naïve Adults, Week 96 Combined Analysis Baseline Characteristics

	E/C/F/TAF n=866	E/C/F/TDF n=867
Age, median years	33	35
Female, %	15	15
Black or African descent, %	26	25
Median HIV-1 RNA, log_{10} c/mL	4.58	4.58
HIV-1 RNA >100,000 c/mL, %	23	23
Median CD4 count, cells/μL	404	406
CD4 count <200, %	13	14
Median estimated GFR_{CG}, mL/min	117	114
Dipstick proteinuria (any grade), %	10	10
Comorbidities, %		
HTN	14	17
DM	3	5

Wohl D, et al; 15th EACS, Barcelona, Spain, October 21-24, 2015; Abst. LBBPD1/1.

Studies 104 and 111: ART-Naïve Adults, Week 96 Combined Analysis Efficacy Outcome (HIV-1 RNA <50 c/mL) at Week 96



- By 96 weeks, VF with resistance occurred in 10/866 (1.2%) in TAF vs. 8/867 (0.9%) in TDF arm
  - 83% (15/18): M184V/I; 2 TAF participants and 3 TDF participants: K65R/N
  - 72% (13/18): primary INSTI-R [TAF] (8) vs. TDF (5)] all genotypically susceptible to dolutegravir

Wohl D, et al; 15th EACS, Barcelona, Spain, October 21-24, 2015; Abst. LBBPD1/1.

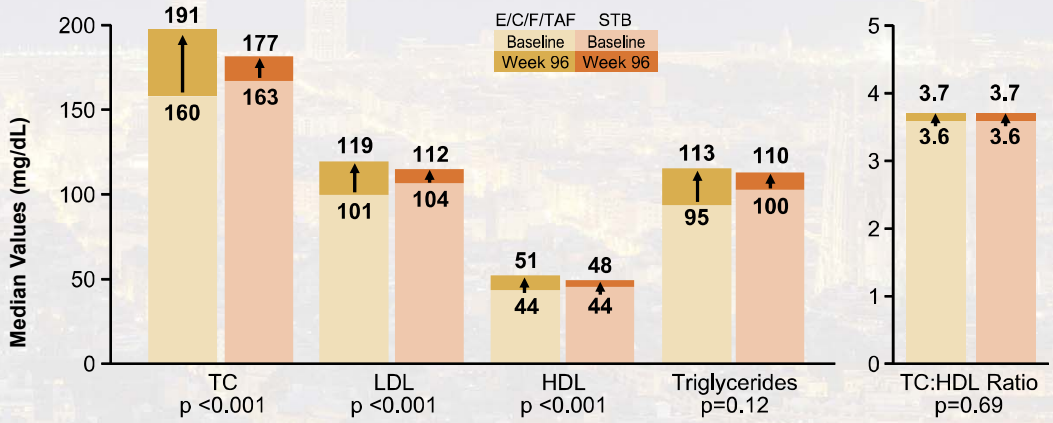
Studies 104 and 111: ART-Naïve Adults, Week 96 Combined Analysis
Common Adverse Events (All Grades)

AEs in ≥10% of Participants, %	E/C/F/TAF n=866		E/C/F/TDF n=867	
	Week 48	Week 96	Week 48	Week 96
Diarrhea	17	+3	19	+4
Headache	14	+3	13	+2
Upper Resp Tract Infection	11	+6	13	+4
Nausea	15	+1	17	+2
Nasopharyngitis	9	+3	9	+3
Cough	8	+3	7	+3
Fatigue	8	+3	8	+2

AE's occurring in at least 10% of subjects in either treatment arm through Week 96

Wohl D, et al; 15th EACS, Barcelona, Spain, October 21-24, 2015; Abst. LBBPD1/1.

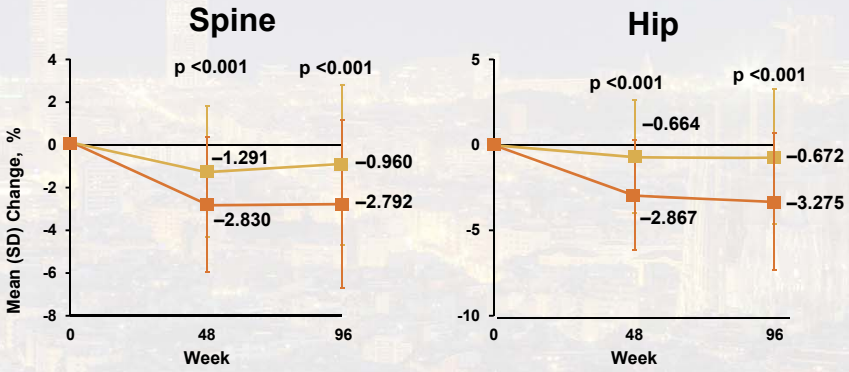
Studies 104 and 111: ART-Naïve Adults, Week 96 Combined Analysis
Fasting Lipids at Week 96



Percentages of subjects who initiated lipid-modifying agents: 3.8% TAF vs 4.4% TDF (p=0.63)

Wohl D, et al; 15th EACS, Barcelona, Spain, October 21-24, 2015; Abst. LBBPD1/1.

Studies 104 and 111: ART-Naïve Adults, Week 96 Combined Analysis
Changes (%) in Spine and Hip BMD Through Week 96

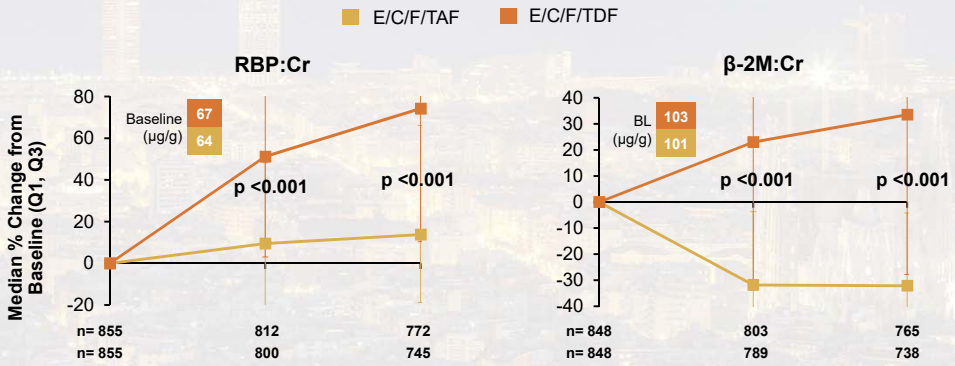


E/C/F/TAF, n	845	795	722	836	791	716
E/C/F/TDF, n	850	790	714	848	784	711

TAF: Less spine and hip BMD loss maintained through week 96

Wohl D, et al; 15th EACS, Barcelona, Spain, October 21-24, 2015; Abst. LBBPD1/1.

Studies 104 and 111: ART-Naïve Adults, Week 96 Combined Analysis
Changes (%) in Quantitative Tubular Proteinuria



- TAF: Decrease in tubular proteinuria sustained to week 96
- E/C/F/TAF: No Fanconi Syndrome or PRT
- E/C/F/TDF: 1 Fanconi Syndrome (discontinuation); 1 subclinical tubulopathy

Wohl D, et al; 15th EACS, Barcelona, Spain, October 21-24, 2015; Abst. LBBPD1/1.