Poster Number

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STaR Study: Single-Tablet Regimen Rilpivirine/Emtricitabine/Tenofovir DF Is Non-Inferior Compared to Efavirenz/Emtricitabine/Tenofovir DF and Improves Patient Reported Outcomes through Week 96

C Cohen[1], D Wohl[2], M Cavassini[3], K Henry[4], M Bloch[5], W Towner[6], W Garner[7], D Porter[7], C Chien[7], S De-Oertel[7]

[1]Comm Res Init of New England, Boston, MA; [2]U North Carolina, Chapel Hill, NC; [3]Ctr Hosp Univ Vaudois, Lausanne, Switzerland; [4]Hennepin County Med Ctr, Minneapolis, MN; [5]Holdsworth House, Darlinghurst, Australia; [6]Kaiser, Los Angeles, CA; [7]Gilead Sciences, Inc., Foster City, CA

Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404
Shampa.De-Oertel@gilead.com

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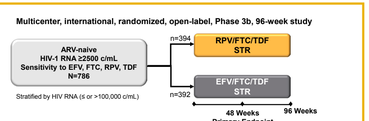
Introduction

- RPV/FTC/TDF is a well-tolerated, once daily single-tablet regimen (STR) treatment option[1,2]
- ECHO and THRIVE established RPV+FTC/TDF as non-inferior to EFV+FTC/TDF in ART-naïve patients
- These studies were blinded, placebo-controlled and used multi-pill regimens which had different food requirements resulting in twice-daily dosing
- STaR is the first head-to-head study to compare the efficacy, safety and tolerability of the two single-tablet regimens, RPV/FTC/TDF and EFV/FTC/TDF
- Patient-reported side effects and symptoms are associated with:
  - Quality of life
  - Physical health
  - Treatment satisfaction
  - Adherence
  - Virologic failure

1. COMPLERA. US Prescribing Information 01/2013. Gilead Sciences, Inc.
2. EVIPLERA. Summary of Prescribing Characteristics 01/2013. Gilead Sciences, Inc.

Methods

Figure 1. Study Design



Primary Analysis
Efficacy of the two STRs by proportion with HIV-1 RNA <50 c/mL at Week 48 (Snapshot analysis); non-inferiority margin of 12%

Secondary Endpoints
Safety and efficacy of the two STRs by proportion with HIV-1 RNA <50 c/mL at Week 96 (Snapshot analysis)
Change in CD4 cell count at Weeks 48 and 96
Genotypic/phenotype resistance at time of virologic failure
HIV Symptom Index Questionnaire
Quality of Life (SF-12, v2)
Treatment Satisfaction Questionnaire

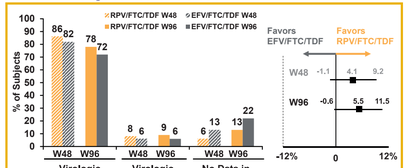
Results

Table 1. Baseline Demographics and Characteristics

	RPV/FTC/TDF n=394	EFV/FTC/TDF n=392
Median age, years (Q1, Q3)	37 (29, 45)	35 (28, 45)
Male	93%	93%
White race	68%	67%
Black race	25%	24%
Latino ethnicity	15%	19%
Mean CD4 cell count, cells/mm³ (SD)	396 (180)	385 (187)
Mean HIV-1 RNA, $\log_{10}$ c/mL, (SD)	4.8 (0.7)	4.8 (0.6)
≤100,000 c/mL, n (%)	260 (66%)	250 (64%)
>100,000 c/mL, n (%)	134 (34%)	142 (36%)
Subjects HBV co-infected, n (%)	13 (3%)*	10 (3%)
Subjects HCV co-infected, n (%)	15 (4%)*	18 (5%)

*Two subjects in the RPV/FTC/TDF arm were co-infected with HIV-1, HBV, and HCV

Figure 2. Virologic Outcomes by Snapshot Analysis and CD4 Change at Weeks 48 & 96

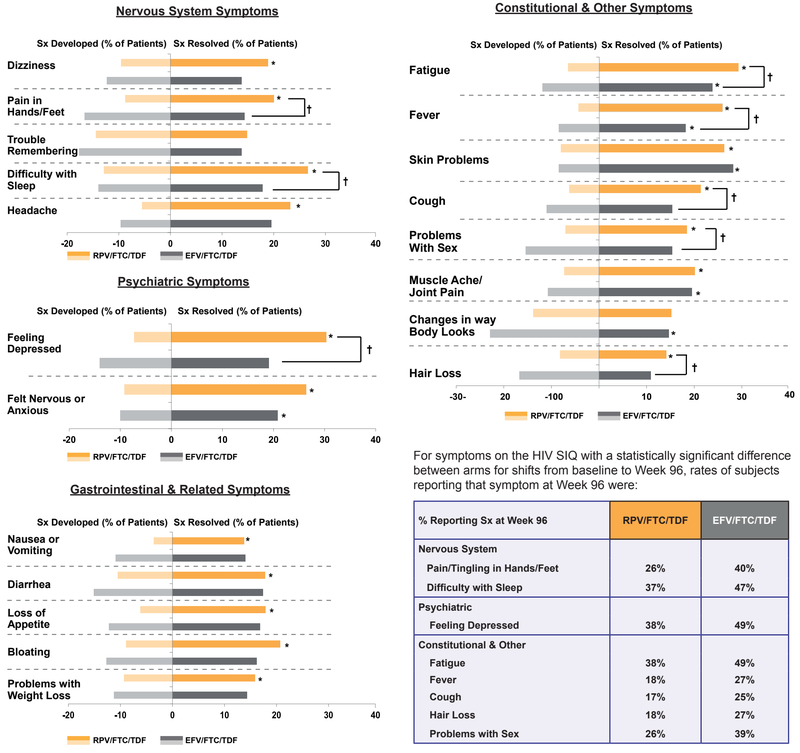


Mean CD4 count change (cells/mm³)
Week 48: RPV/FTC/TDF +200 vs. EFV/FTC/TDF +191 (p=0.37)
Week 96: RPV/FTC/TDF +278 vs. EFV/FTC/TDF +259 (p=0.17)

Results (cont'd)

Figure 3. HIV Symptom Index: Shifts From Baseline at Week 96

Shifts from Baseline
- Sx Developed: subjects who did not have the symptom at baseline but did report it at Week 96
- Sx Resolved: subjects who reported having the symptom at baseline but not at Week 96
- Subjects who had no change in their symptom status are not depicted in the figure

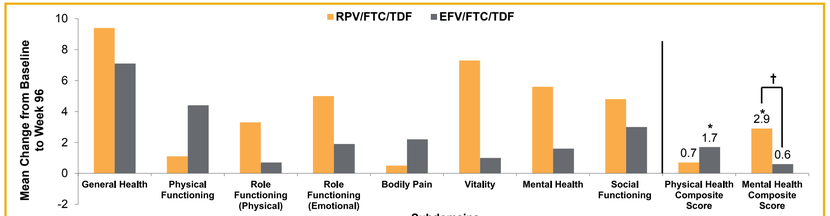


For symptoms on the HIV SIQ with a statistically significant difference between arms for shifts from baseline to Week 96, rates of subjects reporting that symptom at Week 96 were:

% Reporting Sx at Week 96	RPV/FTC/TDF	EFV/FTC/TDF
Nervous System		
Pain/Tingling in Hands/Feet	26%	40%
Difficulty with Sleep	37%	47%
Psychiatric		
Feeling Depressed	38%	49%
Constitutional & Other		
Fatigue	38%	49%
Fever	18%	27%
Cough	17%	25%
Hair Loss	18%	27%
Problems with Sex	26%	39%

* Statistically significant shifts from baseline to Week 96 within each treatment group using the McNemar test
† Statistically significant difference between treatment groups in proportion of patients with shifts from baseline using Cochran-Mantel-Haenszel Row Mean Score test (using modified ridit scores)

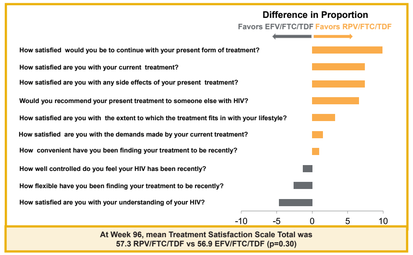
Figure 4. Quality of Life SF-12 (v2) - Changes from Baseline to Week 96



* Statistically significant improvement from baseline (Wilcoxon Signed Rank Test)
† Statistically significant difference between arms (Wilcoxon Ranked Sum Test)

- For the SF-12 (v2), higher scores indicate better quality of life
- For the physical health composite score
  - There were significant improvements from baseline in the EFV/FTC/TDF arm
  - There was no significant difference between groups
- For the mental health composite score
  - There were significant improvements from baseline in the RPV/FTC/TDF arm
  - There was a statistically significant difference between groups favoring RPV/FTC/TDF

Figure 5. Between Group Differences in Proportion of Subjects Responding Most Favorably (Score of 6) to Each HIV Treatment Satisfaction Question at Week 96



At Week 96, mean Treatment Satisfaction Scale Total was 57.3 RPV/FTC/TDF vs 56.9 EFV/FTC/TDF (p=0.30)

Table 2. Grade 3 or 4 Adverse Events and Laboratory Abnormalities through Weeks 48 & 96

	RPV/FTC/TDF n=394		EFV/FTC/TDF n=392	
	BL-W48	W48 -W96	BL-W48	W48 -W96
Treatment Emergent Adverse Events, all Grades	349 (89%)	+13 (3%)	365 (93%)	+3 (0.8%)
Grade 3 or 4 Adverse Events*, n (%)	29 (7%)	+11 (3%)	54 (14%)	+11 (3%)
Grade 3 or 4 Adverse Events of Interest				
Gastrointestinal Disorders	3 (0.8%)	+1 (0.3%)	5 (1.3%)	+2 (0.5%)
Nervous System Disorders	5 (1.3%)	+1 (0.3%)	5 (1.3%)	+1(0.3%)
Psychiatric Disorders	6 (1.5%)	+1 (0.3%)	13 (3%)	+4 (1%)
Skin & Subcutaneous Tissue Disorders	1 (0.3%)	+0	3 (0.8%)	+0
Grade 3 or 4 Laboratory Abnormalities†, n (%)	68 (17%)	+18 (5%)	63 (16%)	+15 (4%)

* Specific events occurring in >1 subject in the RPV/FTC/TDF arm: diarrhea, fatigue, appendicitis, syncope, depression, nephrolithiasis; and in the EFV/FTC/TDF arm: diarrhea, abdominal pain, gastroenteritis, bronchitis, hepatic enzyme increased, headache, pyrexia, convulsion, depression, anxiety, insomnia, suicidal ideation, bipolar disorder, suicide attempt
† Grade 3 or 4 lab abnormalities occurring in ≥1% in the RPV/FTC/TDF arm: ALT, AST, GGT, amylase, neutrophils, creatine kinase, hyperglycemia, glycosuria, hematuria, lipase; and in the EFV/FTC/TDF arm: ALT, AST, GGT, amylase, creatine kinase, total cholesterol, glycosuria, hematuria, neutrophils

Table 3. Adverse Events Leading to Discontinuation of Study Drug through Weeks 48 & 96

	RPV/FTC/TDF n=394		EFV/FTC/TDF n=392		
	BL-W48	W48 -W96	BL-W48	W48 -W96	
Discontinuations* Due to AE, n (%)	10 (3%)	+2 (0.5%)	34 (9%)	+9 (2.3%)	p <0.001**
AE leading to discontinuation in >1 subject in either arm					
Nervous System Disorders	3 (0.8%)	+0	7 (1.8%)	+1 (0.3%)	
Dizziness	0	+0	5 (1.3%)	+1 (0.3%)	
Psychiatric Disorders	1 (0.3%)	+0	18 (5%)	+6 (1.5%)	
Abnormal Dreams	0	+0	4 (1%)	+1 (0.3%)	
Anxiety	0	+0	2 (0.5%)	+0	
Depression	0	+0	7 (1.8%)	+4 (1%)	
Insomnia	1 (0.3%)	+0	3 (0.8%)	+1 (0.3%)	
Nightmare	0	+0	2 (0.5%)	+0	
Suicidal Ideation	0	+0	2 (0.5%)	+1 (0.3%)	
GI, General, Skin Disorders					
Diarrhea	0	+0	2 (0.5%)	+0	
Fatigue	0	+0	2 (0.5%)	+0	
Pyrexia	0	+0	2 (0.5%)	+0	
Toxic Skin Eruption	0	+0	2 (0.5%)	+0	

* per safety population
** p value is for comparison of RPV/FTC/TDF vs EFV/FTC/TDF at Week 96 using Fisher's exact test

Table 4. All Grades Treatment-Emergent Adverse Events of Importance* through Week 96

		RPV/FTC/TDF n=394	EFV/FTC/TDF n=392	
Nervous System Events, n (%)		107 (27%)	186 (47%)	p <0.001
Events ≥5% of subjects	Dizziness	27 (7%)	90 (23%)	
	Headache	56 (14%)	62 (16%)	
	Somnolence	10 (3%)	30 (8%)	
Psychiatric Events†, n (%)		111 (28%)	192 (49%)	p <0.001
Events ≥5% of subjects	Abnormal Dreams	23 (6%)	101 (26%)	
	Anxiety	28 (7%)	37 (9%)	
	Depression	36 (9%)	47 (12%)	
	Insomnia	45 (11%)	59 (15%)	
Rash Events, Overall‡, n (%)		62 (16%)	95 (24%)	p=0.003
Events ≥5% of subjects	Rash	31 (8%)	52 (13%)	

*Prespecified evaluation for common adverse events included in the US Prescribing Information and EMA SmPC for efavirenz, rilpivirine, COMPLERA/EVIPLERA and ATRIPLA®
†One suicide occurred in the EFV/FTC/TDF arm, Day 36 of study
‡The larger category of Rash Events, Overall includes several different types of skin events such as blister, allergic dermatitis, pruritis, and different types of rashes such as macular, pustular, vesicular, etc. Rash falls into this grouping

Conclusions

- Overall RPV/FTC/TDF had non-inferior virologic suppression compared to EFV/FTC/TDF through Week 96
  - Virologic failure rates by Snapshot analysis were 9% for RPV/FTC/TDF and 6% for EFV/FTC/TDF
- On the HIV Symptom Index Questionnaire, there were statistically significant differences between arms in shifts from baseline to Week 96 in:
  - Nervous system symptoms of pain or tingling in the hands or feet and difficulty with sleep
  - Psychiatric symptom of feeling depressed
  - Constitutional and other symptoms of fatigue, fever, cough, hair loss, and problems with sex
- On the Quality of Life SF-12 (v2)
  - There was no significant difference between arms in terms of physical health composite score at Week 96; however in the EFV/FTC/TDF arm there was a significant improvement compared to baseline
  - Subjects in the RPV/FTC/TDF arm showed a significant improvement from baseline as well as a significantly higher score than the EFV/FTC/TDF arm in the mental health composite score at Week 96
- There were similar rates of treatment satisfaction in both arms at Week 96 as measured by the HIV Treatment Satisfaction Questionnaire
- Based on adverse event reports, RPV/FTC/TDF was better tolerated than EFV/FTC/TDF with
  - Significantly lower rates of important nervous system, psychiatric, and rash adverse events common to the EFV and RPV US Prescribing Information and EMA SmPC
  - Significantly lower rates of discontinuations due to adverse events
- Differences in rates of symptoms reported on patient reported outcome measures vs adverse events may be due to
  - The fact that adverse events are spontaneously reported while patient reported outcome questionnaires solicit information about specific symptoms
  - Patient reported outcome questionnaires only address symptoms from the previous 30 days
  - Subjects discontinuing due to adverse events were not included in Week 96 results of patient reported outcome measures

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AUSTRALIA
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Smith, Don

AUSTRIA
Haas, Bernhard
Rieger, Armin
Zangerle, Robert

BELGIUM
Florence, Eric
Van Wijngaerden, Eric
Vandercam, Bernard

CANADA
Angel, Jonathan
Brunetta, Jason
Conway, Brian
Hull, Mark
Lalonde, Richard
Rachlis, Anita
Trottier, Benoit
Walmsley, Sharon

FRANCE
Bollens, Diane
Cotte, Laurent
De Truchis, Pierre
Durant, Jacques
Kattamis, Christine
Molina, Jean-Michel
Pialoux, Gilles
Yeni, Patrick

GERMANY
Arasteh, Kaikaus
Esser, Stefan
Hoffman, Christian
Jäger, Hans
Kern, Winfried
Lutz, Thomas
Rockstroh, Jurgen
van Lunzen, Jan

ITALY
Antinori, Andrea
Lazzarin, Adriano

PORTUGAL
Doroana, Manuela

SPAIN
Arribas, Jose
Gutierrez-Rodero, Felix
Podzamczer, Daniel
Portilla, Joaquin

SWITZERLAND
Cavassini, Matthias
Furrer, Hansjakob

UNITED KINGDOM
Fisher, Martin
Johnson, Margaret
Moyle, Graeme
Orkin, Chloe
Wilkins, Edmund

UNITED STATES
Albrecht, Helmut
Bellos, Nicholaos
Benson, Paul
Berger, Daniel
Bolan, Robert
Brachman, Philip
Brar, Indira
Bredeek, Fritz
Brinson, Cynthia
Burack, Jeffery
Casanas, Beata
Cohen, Calvin
Cook, Paul
Coulston, Daniel
Crelicos, Catherine
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Dejesus, Eduardo
Dejesus, Edwin
deVente, Jerome
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Gathe, Joseph
Gregor-Zantungo, Paola
Grossberg, Robert
Hardy, David
Hawkins, Trevor
Henry, W Keith
Hite, Amy
Hsu, Ricky
Johnson, Marc
Jordan, Wilbert
Towner, William
Vanig, Thanes
Voskuhl, Gene
Weinberg, Barbara
Wells, Charles
Wheeler, David
Wilkin, Aimee
Wohl, David
Wohlfeiler, Michael
Young, Benjamin
Zolopa, Andrew

STaR Study Team
DaCosta, Marilyn

COMPLERA Project Team
Barnett, Sean
Chuck, Susan
Kotecha, Mona
Meyer, Janette
Porter, Danielle
Saba, Dina
Templeton, David
Upchurch, David
Watt, Jennifer

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