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Switching PI to Rilpivirine In-combination with Truvada as a single-tablet regimen Week 24 Results

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Study Design

Switching PI to Rilpivirine In-combination with Truvada as a single-tablet regimen
Multicenter, international, randomized, open-label, Phase 3b, 48-week study

- Stable PI + RTV + 2 NRTIs with HIV-1 RNA <50c/mL ≥ 6 months
- On 1st or 2nd regimen
- No prior NNRTI use
- No known genotypic resistance to study drugs
  (476 treated subjects)

2:1

n=317 → FTC/RPV/TDF STR → FTC/RPV/TDF STR

n=159 → PI + RTV +2 NRTIs → FTC/RPV/TDF STR

24 weeks (Primary Endpoint) — 48 weeks

Primary Endpoint: Non-inferiority (12% margin) of FTC/RPV/TDF to PI+RTV + 2NRTIs by FDA snapshot analysis HIV-1 RNA <50 copies/mL at 24 weeks

Secondary Endpoints:
- Change in fasting lipid parameters
- Safety and tolerability
- Change in CD4 cell count

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Baseline Characteristics & Screening ARVs

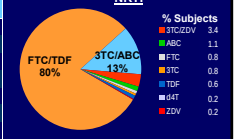
Characteristic	FTC/RPV/TDF N = 317	PI+RTV+ 2NRTIs N = 159
Median age, years (Q1,Q3)	42 (35, 48)	43 (36, 49)
Male, %	86	91
Race, %		
White	76	78
Black	19	14
Ethnicity, %		
Latino	16	20
Median time since first ART, years (IQR)	2.9 (1.9, 4.4)	2.6 (1.7, 4.8)
Mean CD4 cell count, cells/mm³ (SD)	576 (237)	600 (259)

* 3TC, lamivudine; d4T, stavudine; ABC, abacavir; APV, amprenavir; ATV, atazanavir; DRV, darunavir; FPV, fosamprenavir; FTC, emtricitabine; LPV, lopinavir; RTV, ritonarvir; SQV, saquinavir; TDF, tenofovir disoproxil fumarate; ZDV, zidovudine

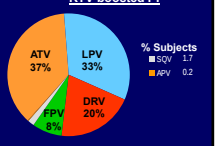
† Includes all treated participants (N =476). 2 participants enrolled not on a boosted PI (protocol violation, enrolled on EFV/FTC/TDF)

Screening ARVs (%)

NRTI*



RTV-boosted PI†



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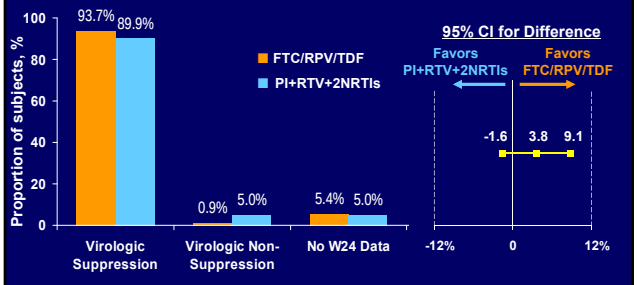
HIV-1 RNA <50 c/mL at Week 24 FDA Snapshot Analysis – ITT Population

Switching to FTC/RPV/TDF was non-inferior to remaining on PI+RTV+2NRTIs



Secondary endpoint of ITT (Missing=Excluded) for HIV-1 RNA <50 c/mL
- **99.7% for FTC/RPV/TDF vs. 94.7% for PI+RTV+2NRTIs**

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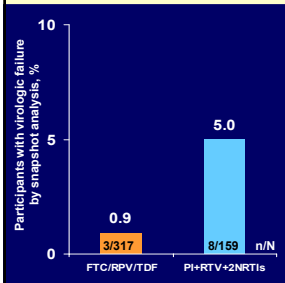
Virologic Non-Suppression HIV-1 RNA >50 c/mL at Week 24 per FDA Snapshot Analysis



- **PI+RTV+2NRTIs (n=8)**
  - **7 with no genotype performed (HIV-1 RNA <400 c/mL)**
  - **1 genotype: M184V**
    - **HIV-1 RNA at analysis 13,300 c/mL**
- **FTC/RPV/TDF (n=3)**
  - **1 with no genotype (VL<400 c/mL)**
  - **1 genotype: M184I**
    - **HIV-1 RNA at analysis 410 c/mL[a]**
  - **1 genotype[b]: M184I, V90I, L100I, K103N**
    - **HIV-1 RNA at analysis 11,900 c/mL[a]**

a. Regimen post study: FTC/TDF+DRV+RTV
b. Protocol violation: 68 wks of prior EFV use with V90I present at baseline

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Grade 3/4 Adverse Events, Laboratory Abnormalities and eGFR Changes

Grade 3 or 4	FTC/RPV/TDF N = 317	PI+RTV+2NRTIs N = 159
Adverse Events	5.0%	6.9%
Laboratory Abnormalities	6.3%*	11.3%†

*≥1% subjects: creatine kinase
†≥1% subjects: creatine kinase, AST, total bilirubin

- **No Grade 3 or 4 adverse event occurred in >1% of subjects in either treatment arm through 24 weeks**
- **Changes in eGFR occurred early and remained stable through Wk 24**
- **eGFR changes from baseline to Wk 24 were greater in the switch arm, -4.4 vs. +0.1 mL/min (p=0.001; ANOVA)[2]**

1. Palella F, et al. IAC 2012; Washington, DC. Oral TUAB0104
2. Data on File. Gilead Sciences

eGFR: estimated glomerular filtration rate by Cockcroft Gault

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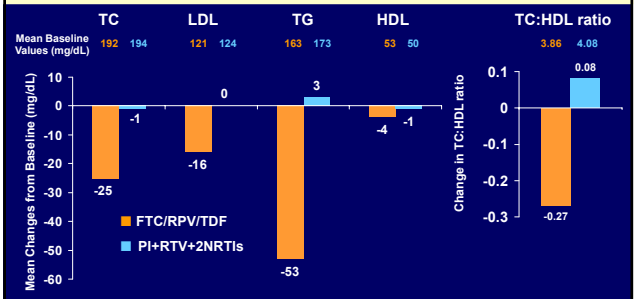
Changes from Baseline to Week 24 in Fasting Lipids



- For all the above lipid parameters, comparisons between treatment groups were statistically different (p<0.001)

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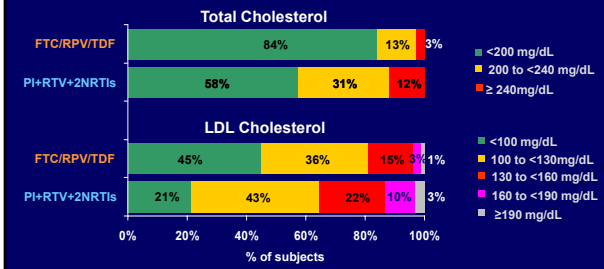
Fasting Total Cholesterol and LDL by NCEP Classification

- At baseline (not shown), no difference in distribution across total cholesterol and LDL NCEP categories comparing FTC/RPV/TDF and PI+RTV+2NRTIs (p=0.93 and p=0.35, respectively)
- At Week 24, statistically significant difference in distribution across LDL and total cholesterol NCEP categories comparing FTC/RPV/TDF and PI+RTV+2NRTIs (p<0.001 for both)



NCEP: National Cholesterol Education Program

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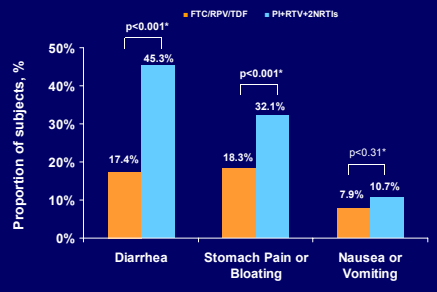
Patient Reported Outcomes at Week 24 per HIV Symptom Index

Gastrointestinal Symptoms



* P-value for comparison between treatment groups at Week 24 using Chi-square

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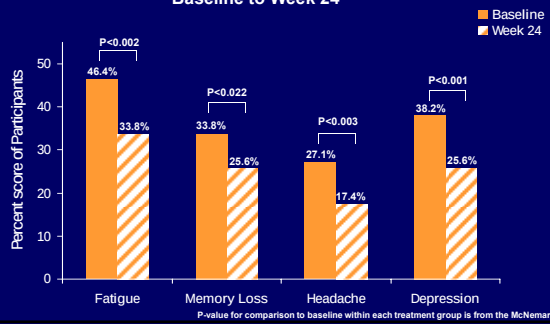
Patient Reported Outcomes at Week 24 per HIV Symptom Index

Improvements per Patient Report for FTC/RPV/TDF Subjects Baseline to Week 24



P-value for comparison to baseline within each treatment group is from the McNemar test

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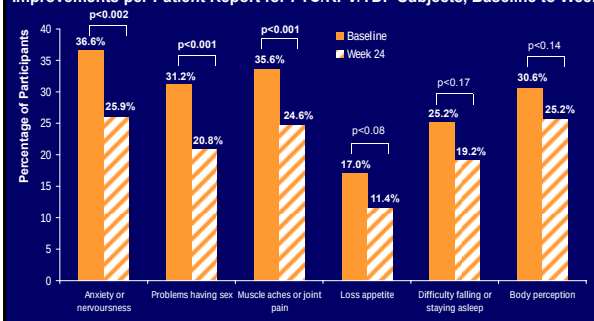
Patient Reported Outcomes at Week 24 per HIV Symptom Index

Improvements per Patient Report for FTC/RPV/TDF Subjects, Baseline to Week 24



P-value for comparison to baseline within each treatment group is from the McNemar test

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HIV Treatment Satisfaction Questionnaire Week 24

How satisfied were you with your current treatment?
How well do you feel your HIV has been controlled recently?
How satisfied are you with any side effects of your present treatment?
How satisfied are you with the demands made by your present treatment?
How convenient have you been finding your treatment to be recently?
How flexible have you been finding your treatment to be recently?
How satisfied were you with your understanding of your HIV?
How satisfied are you with the extent to which the treatment fits into your lifestyle?
Would you recommend your present treatment to someone else with HIV?
How satisfied would you be to continue with your present form of treatment?

Participants that switched to FTC/RPV/TDF reported higher satisfaction with their treatment regimen by HIV-TSQ than persons who remained on PI+RTV+2NRTIs (p<0.001*)

* P-value for comparison between treatment groups at Week 24 from ANCOVA HIV TSQ: HIV Treatment Satisfaction Questionnaire

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Conclusions

- **Through 24 weeks, switching to FTC/RPV/TDF was non-inferior to remaining on PI+RTV+2NRTIs, regardless of baseline HIV-1 RNA[1]**
- **Participants who switched to FTC/RPV/TDF had a lower rate of virologic non-suppression compared to participants remaining on PI+RTV+2NRTIs (0.9% vs 5.0%) at Week 24[1]**
- **Switching to FTC/RPV/TDF resulted in improvement in fasting lipids, including TC, LDL, TGs, and TC:HDL ratio with favorable shifts in NCEP classifications for TC, LDL, and HDL[1,2]**
- **Fewer participants who switched to FTC/RPV/TDF reported symptoms by the HIV Symptom Index[2]**
- **Fewer participants reported symptoms by the HIV Symptom Index2. Greater percentages of FTC/RPV/TDF recipients self-reported satisfaction with their treatment regimen by the HIV-TSQ2**

1. Palella F, et al. IAC 2012; Washington, DC. Oral TUAB0104
2. Tebas P, et al. LIPO 2012; Washington, DC. #018

HIV TSQ: HIV Treatment Satisfaction Questionnaire

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