SPIRIT: Switching to Rilpivirine/Emtricitabine/Tenofovir DF Single-Tablet Regimen fromBoosted Protease Inhibitor Demonstrated High Adherence and High Rates of Virologic Suppression

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8th International Conference on HIV Treatment and Prevention Adherence
Abstract #151
Background

• Regimen simplification
  – improves quality of life\textsuperscript{1-3}
  – increases long-term adherence\textsuperscript{1-3}
  – reduces virologic failure (VF)\textsuperscript{1-3}
  – reduces long-term toxicities\textsuperscript{1-3}

• RPV/FTC/TDF is a well-tolerated, once daily single-tablet regimen (STR) treatment option\textsuperscript{4,5}

• This is the first study to evaluate the safety and efficacy of switching from ritonavir-boosted protease inhibitor (PI+RTV) -based HAART to a simplified regimen of the STR RPV/FTC/TDF in virologically suppressed patients

2. Stone, J Acquir Immune Defic Syndr. 2004;36(3)
3. DHHS Guidelines. February 12, 2013
5. EVIPLERA®. Summary of Prescribing Characteristics 01/2013. Gilead Sciences, Inc.
SPIRIT
Study Design

Switching boosted PI to Rilpivirine in-combination with Truvada as an STR
Multicenter, international, randomized, open-label, Phase 3b, 48-week study

- Stable PI+RTV+2 NRTI ≥ 6 months with HIV-1 RNA <50 c/mL
- On 1st or 2nd regimen
- No prior NNRTI use
- No known resistance to study agents

N=476

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

Secondary Endpoints:
- Proportion of subjects on RPV/FTC/TDF who have HIV-1 RNA <50 copies/mL at Week 48
- Change in fasting lipid parameters and CD4+ cell count at 24 and 48 weeks
- Safety and tolerability to RPV/FTC/TDF at 24 and 48 weeks
- Proportion of subjects who have HIV-1 RNA <50 copies/mL (missing = excluded) through Week 48
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>RPV/FTC/TDF n = 317</th>
<th>PI+RTV+ 2NRTIs n = 159</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (Q1, Q3)</td>
<td>42 (35, 48)</td>
<td>43 (36, 49)</td>
</tr>
<tr>
<td>Male</td>
<td>86%</td>
<td>91%</td>
</tr>
<tr>
<td>White race</td>
<td>76%</td>
<td>78%</td>
</tr>
<tr>
<td>Black race</td>
<td>19%</td>
<td>14%</td>
</tr>
<tr>
<td>Latino ethnicity</td>
<td>16%</td>
<td>20%</td>
</tr>
<tr>
<td>Median time since first ART, years (Q1, Q3)</td>
<td>2.9 (1.9, 4.4)</td>
<td>2.6 (1.7, 4.8)</td>
</tr>
<tr>
<td>Mean CD4 cell count, cells/mm³ (SD)</td>
<td>576 (237)</td>
<td>600 (259)</td>
</tr>
</tbody>
</table>
**SPIRIT**

**Antiretroviral Therapy at Screening**

### NRTI

- **FTC/TDF**: 81%
- **3TC/ABC**: 13%
- **3TC/ZDV**: 3.4%
- **ABC**: 1.1%
- **FTC**: 0.8%
- **3TC**: 0.8%
- **TDF**: 0.6%
- **d4T**: 0.2%
- **ZDV**: 0.2%

### RTV-boosted PI†

- **ATV**: 37%
- **LPV**: 33%
- **DRV**: 20%
- **FPV**: 8%
- **SQV**: 1.7%
- **APV**: 0.2%

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

† Includes all treated participants. 2 subjects enrolled on EFV/FTC/TDF instead of a boosted PI (protocol violation)
Switching to RPV/FTC/TDF was non-inferior to remaining on PI+RTV+2NRTIs for 24 weeks (difference 3.8; 95% CI, -1.6 – 9.1). Similar rates of virologic suppression were also seen with 48 weeks of treatment with RPV/FTC/TDF.

**FDA Snapshot at 24 Weeks**

<table>
<thead>
<tr>
<th>Virologic Suppression (HIV-1 RNA &lt;50 c/mL)</th>
<th>297/317</th>
<th>143/159</th>
<th>140/152</th>
<th>3/317</th>
<th>8/159</th>
<th>2/152</th>
<th>17/317</th>
<th>8/159</th>
<th>10/152</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of Subjects, %</td>
<td>93.7</td>
<td>89.9</td>
<td>92.1</td>
<td>0.9</td>
<td>5</td>
<td>1.3</td>
<td>5.4</td>
<td>5</td>
<td>6.6</td>
</tr>
</tbody>
</table>

**FDA Snapshot at 48 Weeks**

<table>
<thead>
<tr>
<th>Virologic Suppression</th>
<th>283/317</th>
<th>8/317</th>
<th>26/317</th>
<th>297/317</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of Subjects, %</td>
<td>89.3</td>
<td>2.5</td>
<td>8.2</td>
<td></td>
</tr>
</tbody>
</table>

CD4+ mean change (cells/mm³): Week 24, RPV/FTC/TDF immediate switch +20, PI+RTV+2NRTIs +32 (p=0.28), RPV/FTC/TDF delayed switch -7. Week 48, RPV/FTC/TDF immediate switch +10
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Study Drug Adherence

<table>
<thead>
<tr>
<th></th>
<th>RPV/FTC/TDF Immediate Switch (Day 1 – Week 48) n=317</th>
<th>RPV/FTC/TDF Delayed Switch (Week 24 – Week 48) n=152</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean rate of study drug adherence</td>
<td>99%</td>
<td>99%</td>
</tr>
<tr>
<td>Proportion with adherence ≥95%</td>
<td>89.9% (285/317)</td>
<td>92.8% (141/152)</td>
</tr>
</tbody>
</table>

- Adherence was not measured for the PI+RTV+2NRTI arm because drug was not supplied through the study
- Adherence was measured by pill count of returned study medication bottles for the RPV/FTC/TDF arms
- Adherence to the STR RPV/FTC/TDF was high in both arms
SPIRIT
Virologic Outcomes and Change in CD4+ Count for Subjects with ≥95% Adherence*
FDA Snapshot Analysis – ITT Population

*Post hoc analysis

Mean change from baseline in CD4+ count for subjects with ≥95% adherence (cells/mm³): At Week 24, immediate switch +19, delayed switch -13. At Week 48, immediate switch +9
SPIRIT
Virologic Outcomes and Change in CD4+ Count for Subjects with <95% Adherence*
FDA Snapshot Analysis – ITT Population

*Post hoc analysis

Mean change from baseline in CD4+ count for subjects with <95% adherence (cells/mm^3): At Week 24, immediate switch +27, delayed switch +80. At Week 48, immediate switch +22.
Mean Change in CD4+ Count (cells/mm³)
≥95% Adherence: At Week 24, immediate switch +19, delayed switch -13. At Week 48, immediate switch +9
<95% Adherence: At Week 24, immediate switch +27, delayed switch +80. At Week 48, immediate switch +22
Better adherence is associated with lower rates of virologic failure.
Overall, the incidence of Grade 3 or 4 adverse events related to study drug was low in subjects treated with RPV/FTC/TDF. There were no Grade 4 adverse events related to study drug in either adherence strata.
Overall, switching to RPV/FTC/TDF was non-inferior to remaining on PI+RTV+2NRTIs for the primary endpoint of virologic suppression.

There were high rates of adherence for subjects treated with RPV/FTC/TDF.

Better adherence to RPV/FTC/TDF treatment was associated with better efficacy outcomes in terms of higher rates of virologic suppression and lower rates of virologic failure.

Adverse events were low for subjects treated with RPV/FTC/TDF, regardless of adherence rate.
Acknowledgements

We greatly appreciate the involvement of all study subjects, Investigators and their staff, and the SPIRIT Study Team

AUSTRIA
Greil, Richard
Haas, Bernhard
Rieger, Armin
Schalk, Horst
Vetter, Norbert

BELGIUM
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