<table>
<thead>
<tr>
<th>Paper Number</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>P301</td>
<td>Predictors of long-term HIV RNA suppression on darunavir/ritonavir monotherapy in the MONET trial</td>
<td>Arribas, JR*; Pulido, F; Hill, A; van Delft, Y; Moecklinghoff, C (Madrid, Spain)</td>
</tr>
<tr>
<td>P302</td>
<td>A clinical trial to compare the quality of life of HIV+ patients who start monotherapy with LPV/r versus continuing triple therapy with a boosted PI</td>
<td>Pasquau, J*; Hidalgo, C; Vergara, A; Montes, M; Vargas, J; Sanjoaquin, I; Hernandez-Quero, J; Aguirrebengoa, K; Onhuala, F; Rodriguez-Bano, J; Iraz, A; Garcia-Vallecillos, C (Granada, Spain)</td>
</tr>
<tr>
<td>P303</td>
<td>STRIke – characteristics of HIV-1-infected patients treated with a single-tablet regimen in daily clinical practice</td>
<td>Esser, S; Heiken, H; Gallo, L; Schellberg, S*; Schlag, M; Moll, A; Pauli, R; Stoehr, A; Degen, O; Jaeger, H; Stephan, C; Fattkenheuer, G (Martinsried, Germany)</td>
</tr>
<tr>
<td>P304</td>
<td>Monotherapy with boosted protease inhibitors as antiretroviral treatment simplification strategy in the clinical setting</td>
<td>Santos, J; Berrio, D; Miranda, C; Bravo, I; Perez, S; Libre, J*; Paredes, R; Clotet, B; Molto, J (Barcelona, Spain)</td>
</tr>
<tr>
<td>P305</td>
<td>Durability of lopinavir/r monotherapy in people with viral load ≤50 copies/mL</td>
<td>d’Arminio Monforte, A*; Cozzi-Lepri, A; Andreoni, M; di Perri, G; Galli, M; Poli, A; Costantini, A; Maggiolo, F; Viscoli, C; Sghinolfi, L; Rizzardi, G; Bonfanti, P; Gianotti, N; Perno, C; Antinori, A (Milan, Italy)</td>
</tr>
<tr>
<td>P306</td>
<td>Switching to an etravirine regimen in virologically suppressed patients with previous virological failures and presence of resistance mutations</td>
<td>Blanco, J; Casado, J; Gonzalez-Cordoba, A*; Martinez, E; del Palacio, M; Domingo, P; Maitolas, J; Mateo, M; Perez Elias, M; Perez, I; Gutierrez, P; Gaitell, J (Barcelona, Spain)</td>
</tr>
<tr>
<td>P307</td>
<td>Raltegravir 800 mg once-daily is efficacious in already virologically suppressed patients</td>
<td>Ward, D*; Grant, R (Washington DC, USA)</td>
</tr>
<tr>
<td>P309</td>
<td>Lamivudine plus a boosted-protease inhibitor as simplification strategy in HIV-infected patients with toxicity to nucleoside analogues</td>
<td>Casado, J; De la Calle, C; Del Palacio, M; Banon, S; Perez Elias, M*; Moreno, A; Moreno, S (Madrid, Spain)</td>
</tr>
<tr>
<td>P310</td>
<td>Effectiveness and safety of a single-tablet regimen of emtricitabine/efavirenz/tenofovir in HIV-1-infected patients in infectious diseases department</td>
<td>Xerinda, S; Neves, N; Santos, S; Pino, C*; Poinhos, R; Soares, J; Serrao, R; Sarmento, A (Porto, Portugal)</td>
</tr>
</tbody>
</table>

*Indicates presenting author.
Predictors of long-term HIV RNA suppression on DRV/r monotherapy in the MONET trial

Jose Arribas, Hospital la Paz, IdiPAZ, Madrid, Spain, Federico Pulido, Hospital 12 de Octubre, Madrid, Spain, Andrew Hill, MetaVirology Ltd, London, UK, Yvon van Delft, Janssen, Tilburg, Netherlands, Christiane Moecklinghoff, Janssen, Neuss, Germany

Background
In previous studies of protease inhibitor (PI) monotherapy, the inclusion criteria for most clinical trials of PI monotherapy (switch studies) have included:
1. No history of virological failure on PI treatment
2. On stable HAART for 3-6 months, CD4 nadir above 100-200 cells/µL (not in MOST or OK-04 trials)

In other PI monotherapy trials, the predictors of HIV RNA suppression have been:
OK-04 trial: low nadir CD4 count, poor adherence, low baseline haemoglobin
MOST trial: low nadir CD4 count
Abbott 613 trial: low self-reported adherence and HCV baseline CD4 count
MONOI trial: low nadir CD4 count, high pre-treatment HIV RNA, higher baseline HIV DNA, baseline HIV RNA >5 copies/mL
Kalesolo trial: older age

In addition, HCV co-infection is associated with lower HIV RNA suppression rates in a large meta-analysis (Pulido et al, AIDS Reviews 2012, Vol 14).

The Roche Cobas Amplicor assay produces two types of result when the HIV RNA concentration is <50 copies/mL:
1. No HIV RNA detected (Optical density = background); <5 copies/mL
2. Traces of HIV RNA detected (5-50 copies/mL)

During first-line treatment, there is a progressive increase over time in the percentage of patients with HIV RNA <50 copies/mL, and no detectable HIV RNA (e.g. ARTEMIS trial).

ARTEMIS trial: HIV RNA versus time on DRV/r + TDF/FTC (observed data analysis)

The objectives of this study were to identify factors predictive of treatment failure by Week 144:
1. To identify patients most likely to respond to DRV/r monotherapy, to confirm the MONET trial results.
2. To show sustained HIV RNA reductions during DRV/r monotherapy treatment.
3. To conduct an analysis of patients who intensified with NRTIs.

Conclusions
In the MONET trial, patients with baseline HIV RNA <5 copies/mL and HCV negative serology were most likely to show sustained HIV RNA reductions during DRV/r monotherapy treatment.

In the MONET trial, patients with baseline HIV RNA <5 copies/mL and HCV negative serology were most likely to show sustained HIV RNA reductions during DRV/r monotherapy treatment. The sample sizes for some of the subgroups were small. These analyses should be repeated in other PI monotherapy trials, to confirm the patients most likely to respond favourably.

Statistical Methods
Multivariate logistic regression was used to identify factors predictive of treatment failure by Week 144:
- Age
- Sex
- Weight
- Previous PI use
- Hepatitis C antibody status
- Baseline CD4 count
- Nadir CD4 count
- Baseline HIV RNA <5 copies/mL

This analysis was conducted for the primary ITT Switch=Failure population. Additional analyses were conducted (i) for the Per Protocol Population (excluding discontinuations for adverse events or other reasons (ii) including patients who intensified with NRTIs.

By Week 144, HIV RNA <50 copies/mL (ITT, TLOVR, Switch=Failure) was 69% versus 75% in the DRV/r monotherapy and triple therapy arms respectively.

In the Switch Included analysis, HIV RNA <50 copies/mL was 84.0% versus 83.5% in the DRV/r monotherapy and triple therapy arms respectively. In the multivariate analysis for the TLOVR endpoint, positive HCV serology correlated with treatment failure (Odds Ratio (OR) = 2.44, 95% CI 1.20-5.00).

In the analysis including only virological endpoints, both positive HCV serology (OR=2.77, 95% CI 1.18-6.67) and baseline HIV RNA >5 copies/mL (OR=2.78, 95% CI 1.28-6.01) predicted treatment failure.

Results
Week 144:
- HIV RNA <50 HIV RNA at screening and nadir CD4 counts above 100 cells/mm².
- These results cannot be extrapolated to other populations.
- The sample sizes for some of the subgroups were small. These analyses should be repeated in other PI monotherapy trials, to confirm the patients most likely to respond favourably.

Acknowledgements: Thanks to the patients and investigators who participated in the MONET Trial

Presented at: Eleventh International Congress on Drug Therapy in HIV Infection (HIV11), Glasgow, UK, November 2012 [abstract P301]
A clinical trial to evaluate the quality of life of HIV+ patients who start monotherapy with LPV/r versus continuing triple therapy with a boosted PI

Juan Pasquau1, Carmen Hidalgo1, Antonio Verger2, Marisa Montes2, Jorge Verger2, Isabel Sanjoseq1, José Hernández Quero2, Koldo Aguirreba2, Francisco Orihuela2, Jesús Rodriguez-Baño5, Arkaitz Ima2 and Coral García-Velilla1 on behalf of The QoKamón Study Group.


Correspondence: jpasquau@gmail.com

BACKGROUND

The development of antiretroviral drugs has significantly changed the perception of Human Immunodeficiency Virus (HIV) infection and Acquired Immunodeficiency Syndrome (AIDS) from a very fatal to a chronic and potentially manageable disease, and the availability and administration of antiretroviral therapy.

However, despite the great success of highly active antiretroviral therapy (HAART), triple therapy (TT) regimens are associated to long-term toxicity, high costs, and complex administration that may have direct consequences for HIV infected patients because of a decreased treatment adherence, treatment discontinuation, the negative impact caused in quality of life (QoL), and above all because it could affect treatment efficacy.

Since over the past years (LPV/r) as simplification strategy has proved to be less inferior to TT in virological and immunological efficacy.1 In figure, use of simplification to (LPV/r) has been included since January 2006 in treatment guidelines as a therapeutic option for patients with a history of prior protease inhibitor (PI) failure, an unvaluable viral load (≥10,000 copies) by less than 18 months, and signs and symptoms of toxicity from the conventional triple therapy (HIVDR)2.

OBJECTIVE AND DESIGN

Primary objective was to compare the QoL of patients who start LPV/r (ATR) tablets versus patients continuing on TT containing any protease inhibitor (TT) during the first 6 months of LPV/r.

Secondary objective were to assess and compare (ATR) TT versus (LPV/r) on:

• Toxicity evaluation
• Regimen tolerance and safety
• Intriguing/Adherence
• Patient reported outcomes
• QoL changes in the different dimensions

Methods

1. Initial inclusion criteria: Patients were consecutively included in the study from two centers in Spain (Cádiz and Granada) after the 1st visit of the PI. The initial inclusion criteria of the PI were the patients with a history of PI failure, a viral load of ≥10,000 copies for less than 18 months, and signs and symptoms of toxicity from the previous combination therapy.

2. Randomisation: Patients were consecutively included in the study and randomised by an open computer-generated protocol to be treated with ATR or TT. The randomisation was based on the initial place of patient treatment.

3. Dropouts: No patients were lost to follow up after the first 6 months of the treatment.

4. Statistical analysis: The statistical analysis was performed using SPSS 15.0 for Windows. Differences in baseline characteristics were determined using a t-test for continuous variables and the chi-square test for categorical variables. The impact of the treatment on QoL was determined using the Wilcoxon rank test (if normal distribution was not achieved) or the Mann-Whitney test. The QoL impact of the treatment was assessed on the different dimensions of the QoL, using the mean score of each dimension. Differences in QoL were evaluated from the 6th to the 12th month of treatment using the Mann-Whitney test.

5. Ethical considerations: This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and the local institutional ethics committee. The patients were informed of the study's purpose and potential risks. Written informed consent was obtained from all patients.

RESULTS

The results showed that the patients who started on ATR therapy had a significantly lower score on most QoL dimensions compared to patients who continued on TT. The differences were observed in the physical, psychological, and social dimensions of QoL. The differences were significant in all dimensions except for the role functioning dimension.

Conclusions

The results of this study suggest that switching from TT to ATR therapy may improve QoL in HIV+ patients. Further studies are needed to confirm these findings and to evaluate the long-term impact on QoL.

Table 1: Patient baseline characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>ATR (n=76)</th>
<th>TT (n=77)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.3 ± 8.2</td>
<td>47.8 ± 8.1</td>
<td>0.05</td>
</tr>
<tr>
<td>Gender</td>
<td>58 (76%)</td>
<td>61 (79%)</td>
<td>0.42</td>
</tr>
<tr>
<td>CD4 count (cells/mm³)</td>
<td>585 (125-1264)</td>
<td>580 (121-1284)</td>
<td>0.76</td>
</tr>
</tbody>
</table>

Table 2: Patient (%) reducing doses during the previous week to study visit

<table>
<thead>
<tr>
<th>Variable</th>
<th>ATR (n=76)</th>
<th>TT (n=77)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose reduction</td>
<td>31 (41%)</td>
<td>24 (31%)</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Table 3: Clinical variables at final study visit (ATR population)

<table>
<thead>
<tr>
<th>Variable</th>
<th>ATR (n=76)</th>
<th>TT (n=77)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral load (copies/mL)</td>
<td>45 (12-120)</td>
<td>45 (12-120)</td>
<td>0.56</td>
</tr>
</tbody>
</table>

Table 4: QoL impact of the treatment on different dimensions of the QoL

<table>
<thead>
<tr>
<th>Dimension</th>
<th>ATR</th>
<th>TT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical</td>
<td>55.2 ± 20.2</td>
<td>70.3 ± 15.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Psychological</td>
<td>50.8 ± 20.5</td>
<td>68.6 ± 17.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Social</td>
<td>50.1 ± 20.7</td>
<td>68.6 ± 17.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Role functioning</td>
<td>50.1 ± 20.7</td>
<td>50.1 ± 20.7</td>
<td>0.65</td>
</tr>
</tbody>
</table>

Figure 1: Patient distribution

Figure 2: QoL evaluation comparing (LPV/r) versus (ATR) groups (TT population) at final study visit

Figure 3a: ATR score

Figure 3b: ATR percentage of adherent patients

Figure 4: Treatment satisfaction comparing (LPV/r) versus (ATR) groups (TT population) at final study visit

Figure 5: EMIS/BEA (ATR (n=76))

Figure 6: EMIS/BEA (TT (n=77))

Figure 7: EMIS/BEA (TT (n=77))

Figure 8: Treatment satisfaction comparing (LPV/r) versus (ATR) groups (TT population) at final study visit

Figure 9: Treatment satisfaction comparing (LPV/r) versus (ATR) groups (TT population) at final study visit

Table 5: Clinical variables at final study visit (ATR population)

<table>
<thead>
<tr>
<th>Variable</th>
<th>ATR (n=76)</th>
<th>TT (n=77)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral load (copies/mL)</td>
<td>45 (12-120)</td>
<td>45 (12-120)</td>
<td>0.56</td>
</tr>
</tbody>
</table>

Overall, the results of this study indicate that patients who started on ATR therapy had a lower score on most QoL dimensions compared to patients who continued on TT. The differences were observed in the physical, psychological, and social dimensions of QoL. The differences were significant in all dimensions except for the role functioning dimension.
**STRIke – Characteristics of HIV-1 Infected Patients Treated with a Single Table Regimen in Daily Clinical Practice**

S Esser1, H Heiken1, L Gallo1, S Scheibberg1, A Moll1, R Pauli1, A Stoehr1, O Degen1, H Jäger1, C Stapf1, G Falkenheuer1

1University Essen; 2Praxis Georgstraße Hannover; 3Gilead Sciences GmbH; 4Praxiszentrum Kaiserdamm Berlin; 5Gemeinschaftspraxis Isartor München; 6tti Institut, Hamburg; 7UKE Hamburg; 8MVZ Karlsplatz München; 9HIV Center Frankfurt; 10University Cologne

---

**Background**

- The lifelong antiretroviral treatment of HIV-1 infection requires effective and well-tolerated medications complemented by high rates of adherence in order to achieve viral suppression, immunologic restoration and to prevent the development of resistance.

- Single Table Regimens (STR), combining a single antiretroviral agent in one tablet, taken once daily have been designed to achieve high adherence and better long-term outcomes.

- "STRIke" is the first cohort study, describing the use of various STRs in routine clinical practice in Germany, representing a country with predominantly office-based HIV care.

**Methods**

- In this non-interventional observational cohort study 800 participants will be included in 4 treatment arms.

- Patients will be treated with the STRs TDF/FTC/EFV (one retrospective/prospective arm and one purely prospective arm) or TDF/FTC/RPV or - after regulatory approval - TDF/FTC/COBI/EVG.

- Patients are followed prospectively for at least two years, and reasons for change of STR and treatment satisfaction will be collected. In addition to safety, quality of life, demographic and effectiveness data.

**Study Design**

- **Arm 1:** TDF/FTC/EFV retro- and prospective
- **Arm 2:** TDF/FTC/EFV prospective
- **Arm 3:** TDF/FTC/RPV prospective
- **Arm 4:** TDF/FTC/RPV or - after regulatory approval - TDF/FTC/COBI/EVG

**Results**

**Age, Gender, Ethnicity, Mode of Infection**

- Currently Baseline data are available for:
  - Arm 1: 221 patients
  - Arm 2: 162 patients
  - Arm 3: 192 patients

- In general: the spectrum of patients in the study will reflect the usual HIV-1 infected population.

- Gender distribution is very similar in all three arms: 88.3% males in Arm 1; 88.3% males in Arm 2; and 89.5% males in Arm 3.

- The majority of patients are Caucasians: 91% in Arm 1; 87.7% in Arm 2; and 83.5% in Arm 3.

- Patients starting their STR-therapy with TDF/FTC/EFV tend to be slightly younger (mean age 38.7 years) than patients starting with TDF/FTC/RPV (mean age 47.1 years; 4 years respectively).

- Mode of infection in most cases is homosexual contact: 61.8% in Arm 1; 61.8% in Arm 2; and 70.4% in Arm 3 followed by heterosexual contact: 12.2% in Arm 1; 21.4% in Arm 2; and 15.3% in Arm 3.

**Concomitant and Comorbidities at STR start**

- In Arm 1+2, 15.4% of patients had concomitantly at least one comorbid or were treated with other drugs.

**Summary of Regimen Prior to Starting STR**

- In Arm 1, 221 patients started their STR-therapy with TDF/FTC/EFV.

- 87% of patients had prior experience with TDF/FTC/EFV.

- 13% of patients had prior experience with other STRs.

- 10% switched from an NNRTI regimen.

- 28.6% started their STR-therapy following an initial treatment failure with fewer overall comorbidities, but is selected more by younger patients.

- Different STRs may meet the requirements for adherence and better long-term outcomes.

**Regimen Prior to STR**

- Of the 221 patients starting with TDF/FTC/EFV 25% initiated treatment with two PI-STRs, 15% with one PI-STR, and 50% initiated treatment with NNRTI-based STRs.

- Although TDF/FTC/EFV is not approved for naive patients it is used in 73.0% of patients.

- Patients starting with TDF/FTC/EFV as initial therapy was 7% in Arm 1, 14.4% in Arm 2 and 12% in Arm 3.

**Regimen Prior to TDF/FTC/EFV**

- Of the 192 patients starting with TDF/FTC/RPV 25% initiated treatment with two PI-STRs, 15% with one PI-STR, and 50% initiated treatment with NNRTI-based STRs.

- 23.3% of patients in Arm 1 and 2 and 23.3% in Arm 3 had documented relevant comorbidities at STR start.

- Neuropsychiatric disorders and COPD were clearly more common in co-morbid patients, treated with TDF/FTC/EFV.

**Conclusions**

- Single Treatment Regimen aim to make treatment of HIV more convenient, more efficacious and more durable and by that allowing for earlier initiation of treatment.

- Their use in clinical practice, driven by patient preference, appears to meet the requirements for high adherence and mitigation on treatment.

- However, different STRs may meet the requirements of distinct patient populations. TDF/FTC/EFV in this early review of our data, is utilized by younger patients with fewer overall comorbidities, but is selected more frequently for patients with pre-existing neuropsychiatric comorbidities presumably to avoid the known neuropsychiatric complications of TDF/FTC/EFV.

**Acknowledgements**

- The authors wish to thank all participating patients, their partners, the involved investigators and study personnel.

- The clinical trial is sponsored by Gilead Sciences.

---

**Table 3. CDC Stage at STR Start; n=220 Arm 1, n=115 Arm 2, n=119 Arm 3. Missing Data Excluded**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Arm 1</th>
<th>Arm 2</th>
<th>Arm 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (n=197)</td>
<td>15 (7.7%)</td>
<td>10 (6.2%)</td>
<td>23 (12.0%)</td>
</tr>
<tr>
<td>B (n=200)</td>
<td>14 (6.3%)</td>
<td>9 (5.6%)</td>
<td>9 (4.7%)</td>
</tr>
<tr>
<td>C (n=127)</td>
<td>17 (7.7%)</td>
<td>10 (6.2%)</td>
<td>23 (12.0%)</td>
</tr>
</tbody>
</table>

**Table 4. Comorbidities at STR start, n=382 Arm 1+2, n=126 Arm 3**

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Arm 1</th>
<th>Arm 2</th>
<th>Arm 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease (CD)</td>
<td>42%</td>
<td>30%</td>
<td>6%</td>
</tr>
<tr>
<td>Asthmatic disease (AD)</td>
<td>9%</td>
<td>12%</td>
<td>8%</td>
</tr>
<tr>
<td>COPD</td>
<td>10%</td>
<td>7%</td>
<td>1%</td>
</tr>
<tr>
<td>Hypertension (HPN)</td>
<td>10%</td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td>Diabetes mellitus (DM)</td>
<td>5%</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Nephropathy (NPH)</td>
<td>10%</td>
<td>8%</td>
<td>3%</td>
</tr>
<tr>
<td>Chronic hepatitis B (CHB)</td>
<td>5%</td>
<td>4%</td>
<td>2%</td>
</tr>
</tbody>
</table>

**Figure 1. Age in Years at Start of STR-Therapy; n=383 Arm 1+2, n=126 Arm 3**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>n=383</th>
<th>n=126</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 years</td>
<td>150</td>
<td>47</td>
</tr>
<tr>
<td>30-40 years</td>
<td>144</td>
<td>31</td>
</tr>
<tr>
<td>40-50 years</td>
<td>79</td>
<td>35</td>
</tr>
<tr>
<td>&gt;50 years</td>
<td>10</td>
<td>3</td>
</tr>
</tbody>
</table>

---

**Figure 2. Arm 3 Naive Patients; CD4 Cells [cells/mm³] at STR Start, n=126**

<table>
<thead>
<tr>
<th>CD4 Cells</th>
<th>Arm 1</th>
<th>Arm 2</th>
<th>Arm 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;200</td>
<td>73%</td>
<td>71%</td>
<td>75%</td>
</tr>
<tr>
<td>100-199</td>
<td>21%</td>
<td>22%</td>
<td>18%</td>
</tr>
<tr>
<td>&lt;100</td>
<td>6%</td>
<td>7%</td>
<td>7%</td>
</tr>
</tbody>
</table>

---

**Figure 3. NNRTI and PI Regimens Prior to Switching to TDF/FTC/EFV, Arm 1 and 2**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Frequency</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI-only</td>
<td>13%</td>
<td>12%</td>
</tr>
<tr>
<td>PI+NNRTI</td>
<td>87%</td>
<td>88%</td>
</tr>
</tbody>
</table>

---

**Figure 4. NNRTI and PI Regimens Prior to Switching to TDF/FTC/EFV, Arm 3**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Frequency</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI-only</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>PI+NNRTI</td>
<td>97%</td>
<td>97%</td>
</tr>
</tbody>
</table>

---

**Figure 5. Results for STR Start with TDF/FTC/EFV, Arm 3. Multiple Reasons per Patient Possible**

<table>
<thead>
<tr>
<th>Reason for STR Start</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>The decision to start STR therapy on TDF/FTC/EFV was predominantly driven by the decision to simplify ART regimen (73.5%)</td>
<td>81%</td>
</tr>
<tr>
<td>The decision to start TDF/FTC/EFV as STR was driven by the desire to initiate ART with an STR (52.5%)</td>
<td>28.6%</td>
</tr>
</tbody>
</table>

---

**Figure 6. Comorbidities at STR start**

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease (CD)</td>
<td>23%</td>
</tr>
<tr>
<td>Asthmatic disease (AD)</td>
<td>12%</td>
</tr>
<tr>
<td>COPD</td>
<td>4%</td>
</tr>
<tr>
<td>Hypertension (HPN)</td>
<td>7%</td>
</tr>
<tr>
<td>Diabetes mellitus (DM)</td>
<td>5%</td>
</tr>
<tr>
<td>Nephropathy (NPH)</td>
<td>6%</td>
</tr>
<tr>
<td>Chronic hepatitis B (CHB)</td>
<td>2%</td>
</tr>
</tbody>
</table>
Table 2. Reasons for starting monotherapy.a

<table>
<thead>
<tr>
<th>Category</th>
<th>DRV/r-M (n=262)</th>
<th>LPV/r-M (n=311)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47.1 (45.2-52.0)</td>
<td>47.0 (44.0-50.0)</td>
<td>0.096</td>
</tr>
<tr>
<td>HIV co-infection</td>
<td>149 (27.9)</td>
<td>60 (24.8)</td>
<td>0.082</td>
</tr>
<tr>
<td>Time on HIV-1 RNA &gt;50 copies/mL</td>
<td>132 (30.8)</td>
<td>116 (37.0)</td>
<td>0.321</td>
</tr>
<tr>
<td>Time on treatment</td>
<td>10.3 (8.0-14.4)</td>
<td>10.1 (8.6-14.4)</td>
<td>0.994</td>
</tr>
<tr>
<td>No of ART failures</td>
<td>5.0 (4.2-5.8)</td>
<td>5.4 (4.7-6.2)</td>
<td>0.11</td>
</tr>
<tr>
<td>No of ART failure to PI</td>
<td>1.01 (1.0-1.7)</td>
<td>2.0 (1.6-2.4)</td>
<td>0.358</td>
</tr>
<tr>
<td>Any PI resistance</td>
<td>46.0 (43.0-50.0)</td>
<td>45.0 (42.0-48.0)</td>
<td>0.84</td>
</tr>
</tbody>
</table>

aAll values are expressed as No. (%), unless otherwise indicated.

Table 3. Baseline characteristics (n=573) regimens

<table>
<thead>
<tr>
<th>Category</th>
<th>General cohort (n=573)</th>
<th>DRV/r-M (n=262)</th>
<th>LPV/r-M (n=311)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4+ (cells/mm^3)</td>
<td>419 (386-452)</td>
<td>420 (386-452)</td>
<td>0.804</td>
<td></td>
</tr>
<tr>
<td>Time on treatment</td>
<td>10.3 (8.0-14.4)</td>
<td>10.1 (8.6-14.4)</td>
<td>0.994</td>
<td></td>
</tr>
<tr>
<td>No of ART failures</td>
<td>5.0 (4.2-5.8)</td>
<td>5.4 (4.7-6.2)</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>No of ART failure to PI</td>
<td>1.01 (1.0-1.7)</td>
<td>2.0 (1.6-2.4)</td>
<td>0.358</td>
<td></td>
</tr>
<tr>
<td>Any PI resistance</td>
<td>46.0 (43.0-50.0)</td>
<td>45.0 (42.0-48.0)</td>
<td>0.84</td>
<td></td>
</tr>
</tbody>
</table>

aAll values are expressed as No. (%), unless otherwise indicated.

Figure 1. Time to failure according to "on-treatment" and "switch equals failure" analyses (n=573)

Figure 2. DRV/r vs LPV/r monotherapy: on-treatment analysis

Figure 3. DRV/r vs LPV/r monotherapy: switch equals failure analysis

Figure 4. DRV/r vs LPV/r monotherapy: Time to adverse events leading to monotherapy discontinuation

RESULTS

Baseline characteristics:

- We identified a total of 211 and 256 subjects who had initiated DRV/r-M and LPV/r-M monotherapy, respectively, with HIV-1 RNA <50 copies/mL.
- Of these, 51 subjects were consecutively switched from DRV to LPV and 2 more subjects from DRV to LPV.
- Sample comprised 573 monotherapy regimens (262 with DRV and 311 with LPV).
- Overall, the median (IQR) time of follow-up was 65.7 (50.0-141.3) weeks.
- Median (IQR) time of follow-up for DRV/r-M and LPV/r-M were 50 (26-107.6) and 85.6 (38.9-179.1) weeks, respectively (p=0.001).

Overall, 74.5% of patients with PI monotherapy maintained virological suppression at 192 weeks (p=0.095).

Conclusions:

- Overall, only patients whose VL was available up to week 192 were considered, 508/733 (88.7%) subjects maintained HIV-1 RNA <50 copies/mL, and 65/733 (11.3%) experienced VF.
- On VF analysis, 427/733 (57.5%) patients maintained virological suppression at 192 weeks.
- Patients with HIV-infected liver and Peripheral neuropathy were the most common adverse events.

In "OT" analysis, 239/262 (91.2%) patients on DRV/r-M and 272/311 (87.5%) subjects on LPV/r-M maintained virological suppression at 192 weeks (p=0.095).

Safety

- Overall, there were significantly less treatment discontinuations due to adverse events in subjects taking DRV/r-M than LPV/r-M (7.3 vs 22.8%, respectively, p<0.001).
- Adverse events leading to treatment discontinuations were mainly dyslipidemia and gastrointestinal side effects. There were no Grade 3-4 adverse events.

CONCLUSIONS

- Overall, 74.5% of patients with PI monotherapy maintained virological suppression at 192 weeks in routine clinical practice.
- Adverse events leading to treatment discontinuations were mainly dyslipidemia and gastrointestinal side effects. There were no Grade 3-4 adverse events.
**BACKGROUND**

Simplification with PI boosted monotherapy may be a useful strategy in terms of reduction of number of drugs and related toxicities as well as of therapy costs. Several trials have demonstrated that this is a safe approach, at least in selected patients, but now there are no data on the efficacy and toxicity of such simplification regimens in the real world setting.

Although in Italy such regimens are considered *off label*, there is an increasing number of patients who choose this strategy for their treatment. Among these, the most frequent boosted PI used is LPV/r, both because of the data available from clinical trials, and because of its large use among Italian HIV-infected patients.

**OBJECTIVE**

The main objective was to evaluate the durability of LPV/r-monotherapy (MT) in terms of virological rebound (VR), time to discontinuation/intensification or a composite endpoint considering both (=treatment failure).

Secondary objectives were:

- to identify factors associated with faster progression to treatment failure
- to evaluate changes from baseline in plasma lipids and eGFR during follow-up
- to evaluate changes from baseline in CD4 cell count during follow-up
- to evaluate changes from baseline in viral load during follow-up
- to evaluate changes from baseline in tryglicerides during follow-up
- to evaluate changes from baseline in HDL cholesterol during follow-up
- to evaluate changes from baseline in total cholesterol during follow-up

**RESULTS 2: Probability of reaching the different study end-points by 12 and 36 months**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>No. of events</th>
<th>12 months</th>
<th>36 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stop/intensification</td>
<td>24</td>
<td>12.3%</td>
<td>26.0%</td>
</tr>
<tr>
<td>Confirmed VL&gt;100</td>
<td>17</td>
<td>9.2%</td>
<td>17.2%</td>
</tr>
<tr>
<td>Single VL&gt;500</td>
<td>6</td>
<td>3.3%</td>
<td>11.7%</td>
</tr>
<tr>
<td>Single VL&gt;200</td>
<td>24</td>
<td>15.9%</td>
<td>35.5%</td>
</tr>
<tr>
<td>Single VL&gt;100</td>
<td>20</td>
<td>12.1%</td>
<td>30.5%</td>
</tr>
</tbody>
</table>

**Table 1. Main characteristics of the patients stratified by CD4 nadir level**

<table>
<thead>
<tr>
<th>Nucleside pair</th>
<th>H %</th>
<th>Zidovudine/Lamivudine</th>
<th>Abacavir/Lamivudine</th>
<th>Tenofovir/Lamivudine</th>
<th>Didanosine/Lamivudine</th>
<th>Stavudine/Lamivudine</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV RNA &lt; 50 copies/mL</td>
<td>56.4</td>
<td>29.4</td>
<td>56.4</td>
<td>11.8</td>
<td>20.4</td>
<td>11.8</td>
</tr>
<tr>
<td>HIV RNA 50-200 copies/mL</td>
<td>11.8</td>
<td>29.4</td>
<td>11.8</td>
<td>29.4</td>
<td>20.4</td>
<td>11.8</td>
</tr>
<tr>
<td>CD4 count</td>
<td>56.4</td>
<td>11.8</td>
<td>29.4</td>
<td>11.8</td>
<td>20.4</td>
<td>11.8</td>
</tr>
</tbody>
</table>

**RESULTS 4**

- Trend of mean CD4 change from baseline after initiation of LPV/r
- Trend of mean total cholesterol change from baseline after initiation of LPV/r
- Trend of mean HDL change from baseline after initiation of LPV/r
- Trend of mean triglycerides change from baseline after initiation of LPV/r

**CONCLUSIONS**

- In our real-life setting, the KM estimates of reaching a VL suppressed ≤50 copies/mL, by 3 years of starting LPV/r-MT, was 64%. This percentage was >50% when considering only confirmed virological failures.
- The only factor associated with a reduced risk of treatment failure was having switched from previous LPV/r-containing regimens.
- Patients with higher CD4 count nadir and those who had been with a VL≤50 for longer than 1 year before switching to LPV/r-MT tended to be at lower risk of failure.
- CD4 cell count increased by a clinical significant amount after initiation of LPV/r MT.
- We observed an increase in cholesterol/lipids and of eGFR ever following, mainly in the first three months of LPV/r-MT treatment and therefore for this reason we had further investigated additional data.
Simplification of antiretroviral therapy (ART) may be an option for virologically suppressed patients for a variety of reasons. Etravirine (ETV) 400 mg qd has good safety profile and retains activity against viruses resistant to nevirapine or efavirenz.

Our results suggest that ETV plus 2 NRTI could be a good strategy for simplification in virologically suppressed patients despite previous episodes of VF provided that the GSS to the new regimen is >=1.5 and ETV remains active.

We selected patients who were changed from a protease inhibitor (PI) based regimen to ETV plus two NRTIs while virologically suppressed, but that had presented a former virological failure while on NRTIs +/- NNRTIs. A Genotypic Resistance Test performed during previous virological failure had to be available. Eligible subjects were followed for >= 6 months.

Primary endpoint was proportion of patients remaining virologically suppressed using an ITT analysis.

The weight of the GRM was analyzed through a genotypic sensitivity score (GSS) that was calculated summing individual antiretroviral scores obtained through Genotypic Resistance Interpretation Algorithm from the Stanford HIV Drug Resistance Database (0=high-level resistance; 0.5= intermediate-level resistance; 0.75= low-level and potential low-level resistance; 1= susceptible).

Fourteen (10%) of 145 subjects switching to ETV+2NRTIs while virologically suppressed had a documented prior VF and presence of GRM and were included in the analysis.

Median (range) number of previous episodes of VF to ART, NRTI-containing regimen, to a NNRTI-containing regimen and to a PI-containing regimen were 4(1-6), 2(1-5), 1(0-2) and 1(0-2) respectively.

Median duration of virological suppression before switching therapy was 22.5 months (1-65).

All patients switched from an effective PI-containing regimen (8 LPV/r, 5 ATV/r and 1 DRV/r) to a qd regimen with ETV 400 mg plus Truvada® (n=12) or Kivexa® (2).

Eleven out of fourteen patients (79%) remained virologically suppressed at >=6 months. All of them had a GSS >1.5 to the new regimen and none had resistance to Etravirine.

Conversely 3/14 (21%) developed a VF at 1, 3 and 6 months respectively. Two of them had a GSS 1.5 to the new regimen and intermediate resistance to ETV (Y181C). The third one had a GSS 1.75. All these 3 patients had a former VF to a nevirapine containing regimen. No side effects were reported.

Our results suggest that ETV plus 2 NRTI could be a good strategy for simplification in virologically suppressed patients despite previous episodes of VF provided that the GSS to the new regimen is >=1.5 and ETV remains active.
Raltegravir 800 mg Once Daily Is Efficacious in Patients Already Virologically Suppressed

Douglas J Ward, MD, Robert R C Grant, BA
Dupont Circle Physicians Group, Washington, DC, USA

Background:

Raltegravir (Isentress), the first HIV-1 integrase inhibitor, is a potent and very well tolerated antiretroviral. It is a component of a “preferred” regimen in various treatment guidelines for treatment-naive patients, and is a common component of salvage regimens. Its only disadvantage is its twice-per-day dosing. Ever since its initial approval there has been interest in once-daily (800 mg) dosing. QD dosing is certainly more convenient, and may improve adherence. The terminal half-life of raltegravir approaches that necessary for once-daily dosing, where raltegravir 800 mg qd was compared to 400 mg bid, given along with tenofovir/ emtricitabine. In early dose-ranging trials, daily doses substantially lower than the recommended-400 mg bid showed efficacy similar to full doses, suggesting that the lower levels at the end of the dosing interval may still have sufficient potency. In addition, if given with atazanavir, the metabolism of raltegravir by the enzyme UGT A1A is inhibited, resulting in slightly higher drug levels and longer half-life. Once daily dosing was investigated in the QDMerck trial, where raltegravir 800 mg qd was compared to 400 mg bid, given along with tenofovir/ emtricitabine. This trial was stopped after 48 weeks because of an increased rate of virologic failure in those on the qd arm, nNY with the development of integrase resistance. Importantly, however, this trial was performed in treatment-naive patients, and there was a significantly higher risk of virologic failure in those with high baseline PCR (greater than 100,000 c/ml).

Methods:

This is a retrospective review of patients receiving raltegravir 800 mg qd, along with various other combinations of antiretrovirals, in a large HIV-specialty practice. 104 patients were identified taking raltegravir qd who had at least six months of follow-up after starting daily raltegravir. Two patients stopped treatment while on this regimen; their follow-up time is truncated at the time of discontinuation.

Patient Population:

Demographics: (n=104)
Age: Median: 46
Range: 25-76
Sex: Male: 102
Female: 3
Race: Caucasian: 77
Black: 18
Hispanic: 9
Asian: 8
HIV Acquisition:
Homo-sex: 98
Hetero-sex: 7
Status before any antiretroviral therapy:
CD4 count: (n=98)
Mean: 354 (n=98)
Range: 4-961
PCR: (n=70)
Mean: 46,565
Range: 600 – 5,000,000

Other drugs in regimen:
TFV / FTC (Truvada): 69
MRV / TFV / FTC: 2
ABC / STC (Kivexa, Epzicom): 10
ATV / 2 drug regimen: 7
MRV / RLP: 1
ATV / MRV: 7
ATV / MRV / 3TC: 1
ATV / ABC / 3TC (4 drug): 6
3TC = lamivudine, ABC = abacavir, ATV = atazanavir, FTC = emtricitabine, MRV = maraviroc, RLP = rilpivirine, TFV = tenofovir

Time on antiretroviral therapy before QD:
Median: 110 months
Range: 15-304 months

Regimen before QD raltegravir:
Bid Raltegravir containing: 50
Median time on BID RTG: 12 months
Boosted PI: 15
Unboosted PI: 11
Asian: 1
NNRTI: 28

History of treatment failure / documented resistance: 31
Documented mutations (n=29):
M184: 17
K65: 5
TAMS: 14
K103: 6
181: 8
Other NNRTI: 13
PI: 7

Outcomes:

Time on QD Raltegravir:
Median: 27 months
Range: 6-45 months

Most recent PCR:
< 200: 104
< 50: 89
20-200 (“blips”): 15 (all patients with PCR 20-200 have previously been <20)

Two patients on a two-drug regimen of atazanavir/raltegravir had persistent low-grade positive PCRs (50-200 c/ml) and had maraviroc added to the regimen.

Conclusions:

Although this review is small, uncontrolled, and retrospective, it supports the use of raltegravir 800 mg qd in those already on antiretroviral therapy with undetectable viral loads. Although once-daily dosing can not be recommended for those initiating therapy or those with significant antiretroviral resistance, it appears to be sufficient for those already virologically suppressed. For the appropriate patient, once-daily dosing would make raltegravir more convenient, therefore likely increasing adherence and potentially improving outcomes.
Lamivudine plus a boosted-Protease Inhibitor as Simplification Strategy in HIV-infected Patients with Toxicity to Nucleoside Analogues.

José L. Casado, Cristina de la Calle, María del Palacio, Saray Barán, María J Pérez-Elías, Ana Moreno, Santiago Moreno.
Dept of Infectious Diseases, Ramón y Cajal Hospital, Madrid, Spain.

Several studies have shown that a PI/r in monotherapy could be an alternative for the maintenance of virological suppression. However, monotherapy was less effective in case of previous virological failure, or in patients with a low nadir CD4+ count. Therefore, HIV treatment guidelines consider monotherapy as an alternative strategy for patients, virologically suppressed and without previous virological failure, who had toxicity or intolerance to NA. However, in the clinical setting, the management of patients could be more complex. Those developing toxicity could have limited options, because of previous failure, a low nadir CD4+ count, or intolerance to several drugs. In these patients, PI/r-based monotherapy could be a risky strategy. Therefore, dual therapy with lamivudine plus a PI boosted with ritonavir (PI/r) could be an alternative to standard triple therapy or PI/r monotherapy as a simplification strategy in patients with toxicity to nucleoside analogues (NA).

Objective

to determine the efficacy and safety of a simplification strategy to lamivudine plus a PI/r in the clinical setting, in patients with toxicity or intolerance to NA, as an intermediate strategy between mono and triple therapy.

Methods
Retrospective cohort study of 44 HIV-infected patients on suppressive HAART, with no chronic HBV, who simplified to this dual therapy since 2008. Virological and immunological outcome, lipids and renal changes were evaluated. The primary outcome measure was the proportion of patients without therapeutic failure at 48 weeks. Secondary endpoints included toxicity, changes in CD4+ count, and average change in serum lipid levels and renal parameters from baseline to week 48. Patients’ end of follow up was considered the date of regimen change or, if continued, until 31st July 2012.

Results

Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex (%)</td>
<td>29 (66%)</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>40 (38-70)</td>
</tr>
<tr>
<td>Median time of HIV infection (years)</td>
<td>16.8 (4.8-20.4)</td>
</tr>
<tr>
<td>Prior diagnosis of AIDS</td>
<td>23 (55%)</td>
</tr>
<tr>
<td>Former IDU as risk practice</td>
<td>35 (80%)</td>
</tr>
<tr>
<td>Median CD4+ count nadir (cells/μL)</td>
<td>150 (4-470)</td>
</tr>
<tr>
<td>Mean number of previous HAART regimens (failure/intolerance)</td>
<td>4 (2-20)</td>
</tr>
<tr>
<td>Median CD4+ count nadir (cells/μL) at inclusion</td>
<td>403 (145-927)</td>
</tr>
<tr>
<td>Median time on suppressive, PI/r-based HAART (days)</td>
<td>784 (235-2344)</td>
</tr>
</tbody>
</table>

P/r-based HAART:
- Darunavir: 26 (57%)
- Lopinavir: 14 (32%)
- Atazanavir: 5 (11%)

NA discontinued:
- Tenofovir: 19 (43%)
- Didanosine: 15 (34%)
- Abacavir: 3 (7%)
- Zidovudine: 6 (11%)
- Stavudine: 2 (5%)

Previous resistance test: Genotypic mutations

<table>
<thead>
<tr>
<th>NA</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNRTI</td>
<td>4</td>
</tr>
<tr>
<td>NRTI</td>
<td>7</td>
</tr>
<tr>
<td>-210W</td>
<td>4</td>
</tr>
<tr>
<td>PI</td>
<td>8</td>
</tr>
</tbody>
</table>

Only two patients failed (5%) at 48 weeks, and no more failures in 62.8 patients-year of follow up.

CD4+ count increased by 55 cells/mm

Mean fasting lipid parameters after dual therapy initiation

Renal function evolution during dual therapy

Mild improvement in eGFR after NA withdrawal, albeit it was not statistically significant (p=0.1)

Dual therapy with lamivudine plus a boosted-PI is safe and effective as simplification strategy in patients with toxicity to NA. This combination could be an alternative to mono or triple therapy in hard to treat patients, although an initial increase in lipid parameters could be observed.
Evaluate the effectiveness and safety of simplification of tenofovir/emtricitabine/efavirenz (TDF/FTC/EFV) in selected treatment-experienced HIV-1 infected patients who have been virologically suppressed for > 3 months on their current regimen.

METHODS

We selected patients who started the simplified regimen between December 1st 2008 and March 31st 2012. Exclusion criteria: prior therapeutic failure, presence of resistance mutations to any of TDF/FTC/EFV component and patients previously observed in other centers. Efficacy and safety assessments were performed at baseline, 4 weeks after switch and then every 12-24 weeks. Statistical analysis performed with SPSS version 20.0.

RESULTS

- CD4 cell count: 504/mm³ (367-710)
- Glomerular filtration rate (eGFR; Cockcroft-Gault equation): 100 mL/min (86-116)
- ALT: 33 U/L (21-47)
- Total cholesterol (TC): 205 mg/dL (176-236)
- High density lipoproteins (HDL): 45 mg/dL (38-54)
- Low density lipoproteins (LDL): 130 mg/dL (108-151)
- Triglycerides (TG): 125 mg/dL (84-176)

Occurrence of blips° was documented in 98 (26%) patients

In 70 the VL decreased to < 20 copies/mL after the blips
In 28 VL is not yet available

° transient increase in viral load (VL) ≤ 200 copies/mL

CONCLUSIONS

✓ Simplification to TDF/FTC/EFV was shown to be an efficient and safe option in virologically suppressed patients and without a previous virological failure.
✓ Compared with baseline, significantly higher levels of CD4 cells count, HDL and eGFR were found as well as lower levels of TC, LDL and TG.