Outcomes of protease inhibitor Darunavir / Ritonavir (DRV/r) monotherapy in a clinical setting

R. Castles, C. Pacho, J. Swan, S. Sonecha, M. Nelson
St Stephen’s Centre, Chelsea and Westminster Hospital, London, UK

Introduction

- Regimen simplification may help reduce pill burden, enhance tolerability, and cut costs (1).
- Since adherence to antiretroviral medicines (ARVs) is pivotal to successful treatment of HIV (3) the potential benefits of simplification are great.
- Protease inhibitor (PI) monotherapy is one of a number of different simplification strategies.
- The MONET and MONOI trials have studied the use of DRV/r monotherapy and have shown DRV/r to have comparable antiviral efficacy when compared with triple therapy and a potential for a reduction in pill burden, toxicity and cost (2,3).
- Ongoing studies are looking at monotherapy as a viable ARV option for HIV infected patients and it is in use locally for specific individuals. It is not currently a standard of care in BHIVA guidelines.
- We measured treatment outcomes for patients treated at our centre with DRV/r monotherapy and investigated reasons why treatment with monotherapy was stopped.

Method

- All patients commenced on DRV/r (800mg/100mg) monotherapy between 1st January 2008 and 1st January 2011 were identified using our local electronic patient record (EPR system).
- A snapshot was taken at 30th June 2011 to identify how many of these patients were continuing on DRV/r monotherapy at this time point.
- The EPR system and electronic communication notes were used to review virological outcomes in all patients and to identify reasons for cessation of treatment in patients no longer on DRV/r monotherapy.

Results

- 232 patients were commenced on DRV/r monotherapy between January 2008 and January 2011.
  - The average CD4 count for the population was 499 (range: 14 -1,399) at baseline
  - 12% had a detectable viral load (VL > 200 copies RNA/ml) with an average VL of 32,239 copies RNA/ml (range: 213 – 246,621) at baseline
- At 30th June 2011, 178 patients remained on DRV/r after a mean of 16 months of therapy (range 6 - 42 months), of which 84% had a suppressed viral load (< 200 copies RNA/ml).
- 49 patients had stopped monotherapy after a mean of 10 months (range 1 - 32 months). Table 1 illustrates the reasons for stopping.
  - VL increase was the most common reason for stopping DRV/r monotherapy (n=22).
  - 21 of the 22 patients that had stopped due to VL increase had their regimens intensified by addition of another ARV agent and one patient had a complete change of regimen.
  - Figure 1 illustrates the most commonly used ARVs to intensify:
    - 17 used NRTIs, 2 used NNRTIs and 2 used Maraviroc
  - Truvada was the most common combination product and Lamivudine the most common single agent.
  - 19 of the 21 became virologically undetectable after intensification. The patient who changed regimen did not achieve an undetectable VL.
  - Resistance tests were reviewed, where available, in those patients who stopped due to viraemia. No new PI resistance was detected.
  - ADRs were the 2nd most common reason for cessation of treatment. Table 1 illustrates the most common complaints were related to GI symptoms and weight gain.

Table 1. Reasons for discontinuation

<table>
<thead>
<tr>
<th>Reason for stopping DRV/r</th>
<th>N=49 (%)</th>
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</thead>
<tbody>
<tr>
<td>VL increase</td>
<td>22 (45%)</td>
</tr>
<tr>
<td>ADRs</td>
<td></td>
</tr>
<tr>
<td>G.I.*</td>
<td>6 (12%)</td>
</tr>
<tr>
<td>Weight gain</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Non-specific toxicity</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>CNS</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Skin reaction</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Patient Preference</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Planned intensification**</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td></td>
</tr>
<tr>
<td>Inadequate response</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Non-compliance</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Drug interactions</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>RIP</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

** GI includes nausea, vomiting, stomach pain and diarrhoea.
** Planned intensification of regime having temporarily been on monotherapy due to acute illness.

Figure 1.

Conclusions

- This study shows that DRV/r monotherapy is effective in the majority of individuals reviewed.
- The main reason for patients stopping DRV/r is increase in viraemia which in most cases was successfully managed by regimen intensification.
- This suggests that monotherapy may be an effective, safe and potentially cost saving antiretroviral treatment option in select patients.
- More data are required regarding clinical and long-term virological outcomes, the PIVOT study results should help provide this.

References