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

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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 (2) 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 (3,4)
- 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

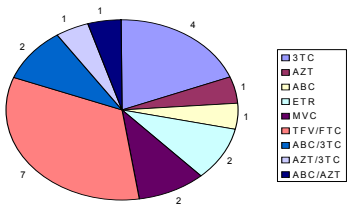
- 232 patients were commenced on DRV/r monotherapy between January 2008 and January 2011.
  - The average CD4 count for the population was 499 (range: 14 -1,399) at baseline
  - 12% had a detectable viral load (VL > 200 copies RNA/ml) with an average VL of 32,239 copies RNA/ml (range: 213 – 246,621) 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

Reason for stopping DRV/r		N=49 (%)
VL increase		**22** (45%)
ADRs	Total	**15** (30%)
	G.I.*	**6** (12%)
	Weight gain	**3** (6%)
	Non-specific toxicity	**2** (4%)
	CNS	**2** (4%)
	Skin reaction	**2** (4%)
Patient Preference		**4** (8%)
Planned intensification**		**3** (6%)
Miscellaneous	Inadequate response	**1** (2%)
	Non-compliance	**1** (2%)
	Unknown	**1** (2%)
	Drug interactions	**1** (2%)
	RIP	**1** (2%)

* 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

1) Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. U.S. Department of Health and Human Services. (2009) Available online: http://aidsinfo.nih.gov/Guidelines/HTML/1/adult-and-adolescent-treatment-guidelines/16/regimen-simplification

2) British HIV Association guidelines for the treatment of HIV-1-infected adults with antiretroviral therapy 2008. HIV Medicine (2008), 9, 563–608.

3) Arribas JR, Horban A, Gerstoft J, et al. The MONET trial: darunavir/ritonavir with or without nucleoside analogues, for patients with HIV RNA below 50 copies/ml. *AIDS*. 2010;24(2):223-230.

4) Katlama C, Valentin MA, Algarte-Genin G, et al. Efficacy of darunavir/ritonavir as single-drug maintenance therapy in patients with HIV-1 viral suppression: a randomized open-label noninferiority trial, MONOI-ANRS 136. AIDS. 2010;24(15):2365–2374.

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