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Poster presentation



# Simplification from TPV/RTV 500/200 BID to TPV/RTV 500/100 BID guided by therapeutic drug monitoring

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## Background

Tipranavir/ritonavir (TPV/r) is a potent protease inhibitor (PI), whose most frequent grade 3/4 toxicity is ALT, AST and lipids elevations. These alterations seem to be associated to TPV exposure, being lower with TPV/r 500/100 mg BID than using TPV/r 500/200 mg BID. Therefore, the tolerance of TPV/r could be improved by reducing ritonavir dose; however, this strategy could be adequate as long as the virological response is not compromised. In this regards, therapeutic drug monitoring (TDM) of TPV could be helpful.

## Methods

A prospective study was initiated in HIV antiretroviral-experienced patients with plasma HIV-RNA <50 copies/mL under a TPV/r 500/200-based regimen for longer than 24 weeks. Patients were randomized to stay on the same TPV/r dosing or to switch to TPV/r 500/100 BID. TPV plasma trough concentrations had to be above the Cmin (≥20.5 ug/mL) before recruitment in the study. Lipids and liver enzymes were recorded at baseline and at week 12 of follow-up. TPV Ctrough was measured using a validated HPLC-UV.

## Summary of results

A total of 10 patients were recruited in the study, five on TPV/r 500/200 BID and five on TPV/r 500/100 BID. All were male; mean [range] age, 45 [40–54] years; CD4 count, 550 [390–646] cells/μl; AST, 36 [20–83]; ALT, 29 [16–140]; total cholesterol, 205 [179–261]; triglycerides, 134 [104–384]. While TPV Ctrough at week 12 remained significantly unchanged in patients on stable TPV/r 500/200 BID, all patients switched to TPV/r 500/100 BID experienced a drop in TPV Ctrough ranging from 9 to 30%.

Four out of five patients switched to TPV/r 500/100 showed a decline in AST, ALT and total cholesterol (drop ranging from 5 to 45%, 15 to 49%, and 2 to 22%, respectively). In contrast, triglycerides only diminished in two patients (7% and 61%, respectively). In all five patients, plasma HIV-RNA remained undetectable at week 12. However, three patients showed sub-therapeutic TPV Ctrough and accordingly treatment was modified. The other two patients have maintained undetectable viral load with similar benefit in lipids and liver enzymes over 12 months of follow-up.

## Conclusion

A subset of antiretroviral-experienced patients on successful TPV/r 500/200 BID based regimens could benefit from ritonavir dose reductions, which may be associated with improvements in liver enzymes and lipids. However, due to large inter-individual differences in TPV Ctrough, this strategy should only be performed using TDM. (Table 1.)

**Table 1:**

| Pts. | Concomitant ARV | Major mutations | HCV | Baseline (TPV500/ RTV200) | | | | | Week 12 (TPV500 / RTV100) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | TPV Ctrough | AST | ALT | Cholesterol | Triglycerides | TPV Ctrough | Therapeutic Levels | AST | ALT | Cholesterol | Triglycerides |
| 1 | ABC 3TC AZT | 10 V, 47 V, 54 V | Yes | 45,4 | 83 | 140 | 179 | 134 | ↓ 17% | Yes | ↓ 45% | ↓ 49% | ↓ 9% | ↓ 7% |
| 2 | TDF FTC RAL | 84 V | No | 37,5 | 20 | 16 | 261 | 127 | ↓ 30% | No | ↑ 50% | 0% | ↓ 13% | ↑ 25% |
| 3 | TDF FTC RAL | No data | No | 24,9 | 20 | 27 | 194 | 104 | ↓ 18% | No | ↓ 5% | ↓ 15% | 0% | ↑ 123% |
| 4 | TDF FTC | None | No | 29,6 | 37 | 73 | 245 | 384 | ↓ 14% | Yes | ↓ 19% | ↓ 49% | ↓ 22% | ↓ 61% |
| 5 | ABC 3TC AZT | None | No | 22,8 | 24 | 29 | 205 | 229 | ↓ 9% | No | ↓ 33% | ↓ 35% | ↓ 2% | ↑ 40% |

Outcome in antiretroviral-experienced HIV patients on TPV/r switched from 500/200 to 500/100 BID.