

# The pharmacokinetics (PK) of lopinavir/ritonavir (LPV/r) 533/133 mg *b.i.d* plus nevirapine (NVP) (200 mg *b.i.d*) in adult HIV-1 infected individuals

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## BACKGROUND

Interest in NRTI sparing regimens to treat antiretroviral naive patients has increased due to concern over the long term side effects associated with NRTI treatment.

The combination of LPV/r and NVP offers a regimen with a low pill burden and a high genetic barrier to resistance<sup>1</sup>.

However, studies performed in HIV-1 infected adult and paediatric patients revealed a decrease in LPV trough concentrations with co-administration of NVP<sup>2,3</sup>. This interaction is based on the common metabolism of all three drugs by CYP3A and could be explained by induction of CYP3A by NVP<sup>4,5</sup>.

Consequently, a 33% increase of LPV/r dosage to 533/133 mg (4 capsules *b.i.d*) from the standard dose of 400/100 mg (3 capsules *b.i.d*) is recommended in combination with NVP<sup>4</sup>.

## OBJECTIVES

To examine the pharmacokinetics of LPV/r (533/133 mg *b.i.d*) in combination with NVP (200 mg *b.i.d*).

## METHODS

15 HIV infected adults, naive to NNRTI and PI treatment, received LPV/r (533/133 mg *b.i.d*) and NVP (200 mg *q.d*) for 2 weeks followed by NVP 200 mg *b.i.d*.

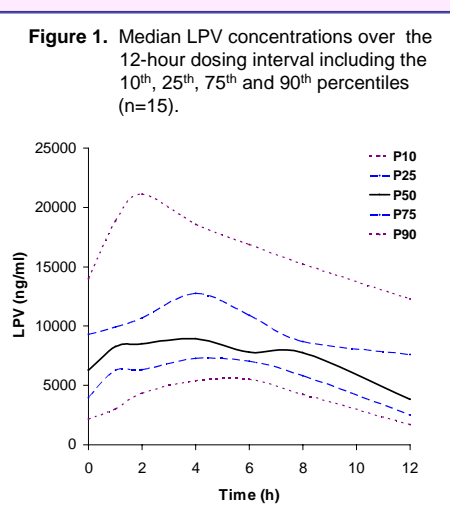
Blood samples were collected pre-dose (0h), 1, 2, 4, 6, 8, 12 hour post-dose.

LPV and RTV plasma concentrations were determined by HPLC-MS/MS and NVP concentrations by HPLC-UV.

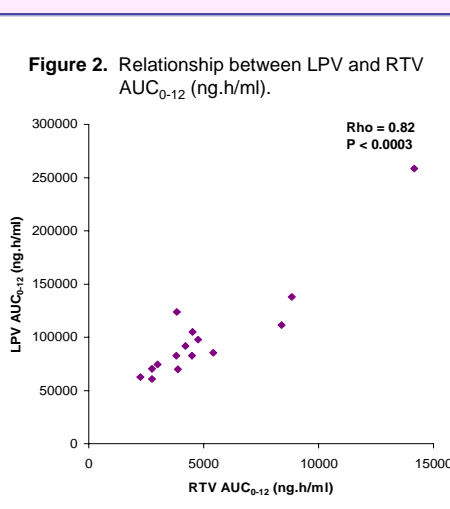
Steady state PK parameters (at week 4) and estimates of population percentiles were derived using non-compartmental analysis (WinNonlin).

## RESULTS

Median LPV  $C_{trough}$  and  $AUC_{0-12}$  [(IQR, CV%)] were 3805 ng/ml [(2510-7613), 77%] and 85588 ng.h/ml [(70190-111347), 48%] (Figure 1).



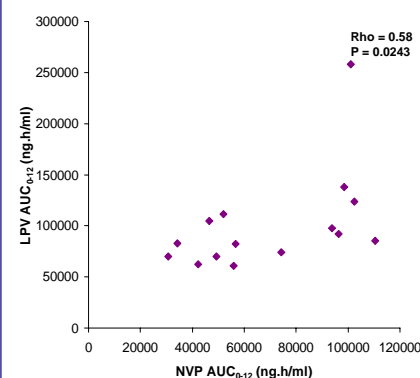
There was a strong positive linear correlation between the  $AUC_{0-12}$  of LPV and RTV (Rho=0.82,  $P < 0.0003$ ; Spearman's rank correlation) (Figure 2).



A positive correlation was observed between NVP and LPV  $AUC_{0-12}$  (Rho=0.58,  $P=0.0243$ ) (Figure 3).

There was only a weak correlation between RTV and NVP  $AUC_{0-12}$  (Rho=0.50,  $P=0.0582$ ).

Figure 3. Relationship between LPV and NVP  $AUC_{0-12}$  (ng.h/ml)



14 of the 15 patients maintained LPV trough levels above the previously reported minimum target trough concentration for treatment naive patients with wild-type HIV-1 (1000 ng/ml)<sup>6</sup>.

## CONCLUSIONS

An increase in LPV/r dosage to 533/133 mg (4 capsules *b.i.d*) is appropriate when used in combination with NVP. However, given the high inter subject variability in LPV trough concentrations the use of TDM is recommended.

A decrease in LPV exposure was not associated with increasing NVP concentrations. In contrast, high LPV/r concentrations were correlated with high NVP concentrations. Further studies which determine intracellular/unbound NVP concentrations and the drug's complete inductive profile are necessary in order to provide more meaningful information regarding this interaction.

We await data for the new tablet formulation of LPV/r in the presence of NVP.

## REFERENCES

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