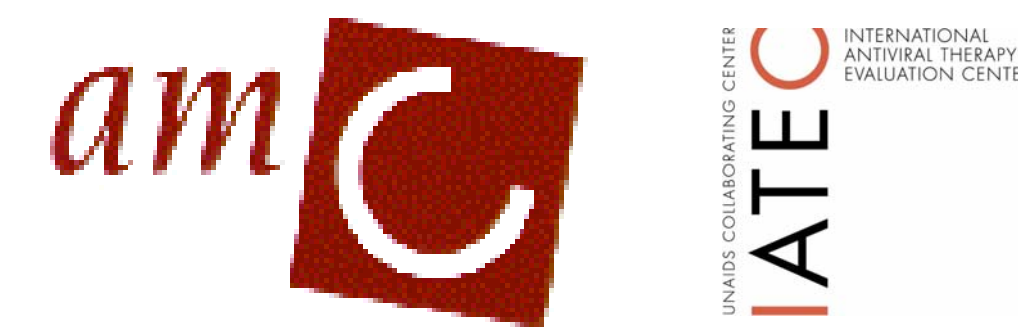


439-W: Penetration of Lopinavir into the Genital Tract of HIV-1 Infected Men

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Background

The decline of the HIV-1 RNA concentration and the evolution of virus in semen during therapy can show discordance with blood plasma, indicating viral compartmentalization. Poor penetration into the male genital tract by some antiretroviral drugs can contribute to the different viral dynamics in this compartment.

Data available on drug concentrations in semen show that the penetration of the protease inhibitors (PIs) nelfinavir, ritonavir and saquinavir is poor. The nucleoside analogues (NRTIs) zidovudine, stavudine, lamivudine and abacavir, the non-nucleoside reverse transcriptase inhibitors (NNRTIs) nevirapine and efavirenz and the PIs indinavir and amprenavir penetrate well into the male genital tract.

There are no data on the penetration of the PI lopinavir (LPV) into the male genital tract. In this study we evaluated whether LPV penetrates into the male genital tract and whether there is suppression of HIV-1 RNA in seminal plasma during antiretroviral therapy including LPV.

Methods

Fourteen HIV-1 infected patients, who were on a LPV containing regimen for at least 4 weeks were included in this study. Semen samples were obtained by masturbation and were centrifuged between 2-4 hours after collection at 1200 g for 10 minutes to obtain seminal plasma (SP). Within 2 hours after semen collection a blood sample was taken for the measurement of the blood plasma (BP) LPV and HIV-1 RNA concentrations.

HIV-1 RNA in BP was measured using the quantiplex bDNA assay (Bayer Corporation, Diagnostics Division Emeryville, CA, USA), with a lower limit of quantification (LLQ) of 50 copies/mL.

HIV-1 RNA in SP was measured using the ultra Nuclisens HIV-1 QT assay (Organon Teknika, Boxtel, The Netherlands), with a LLQ of 50 copies/mL.

LPV concentrations in heparinized BP and in SP were measured using a high-performance liquid chromatographic (HPLC) procedure. The intra and interday variation of this assay is less than 5%.

Figure 1a: LPV concentrations in BP

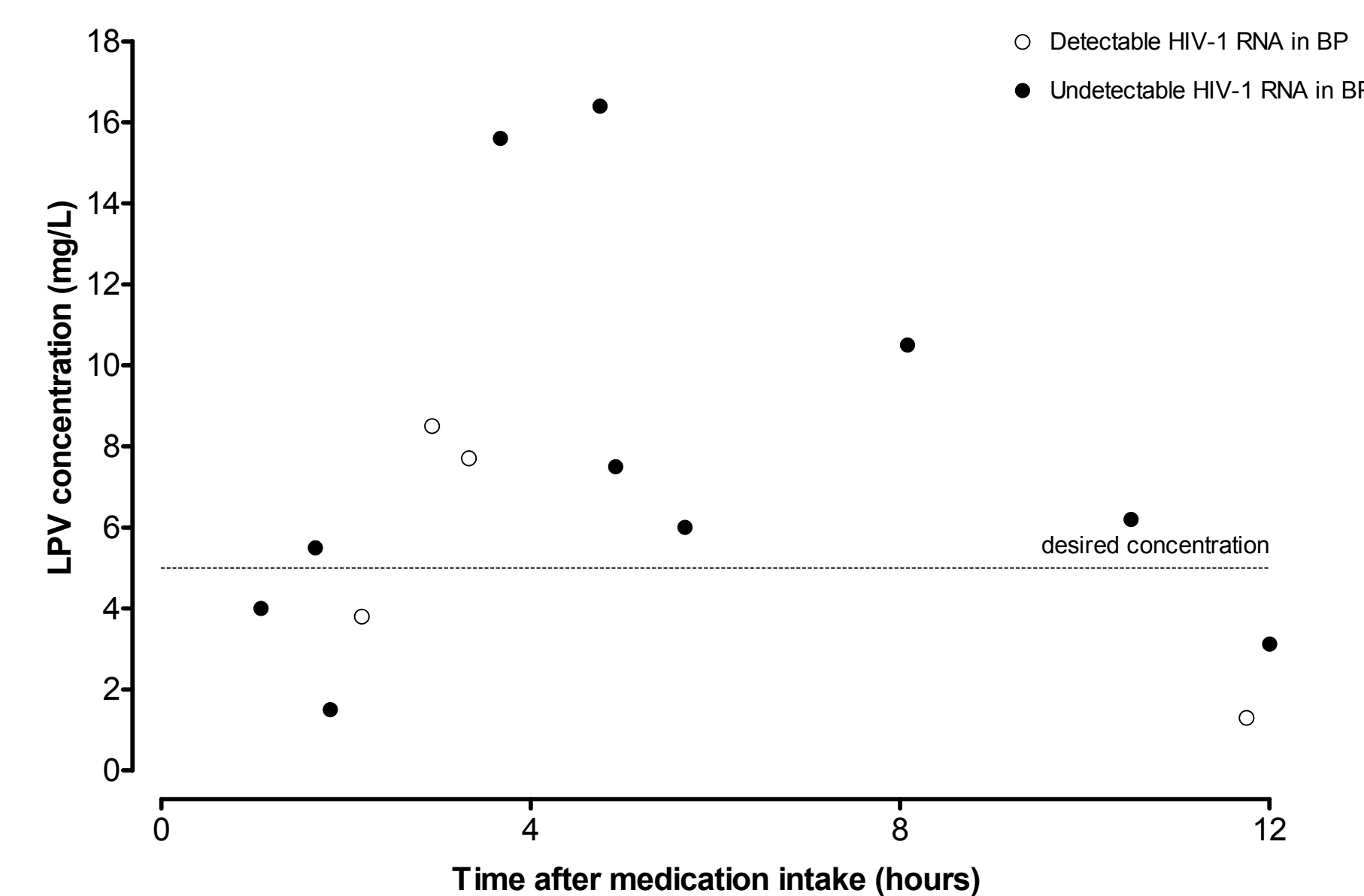


Figure 1b: LPV concentrations in SP

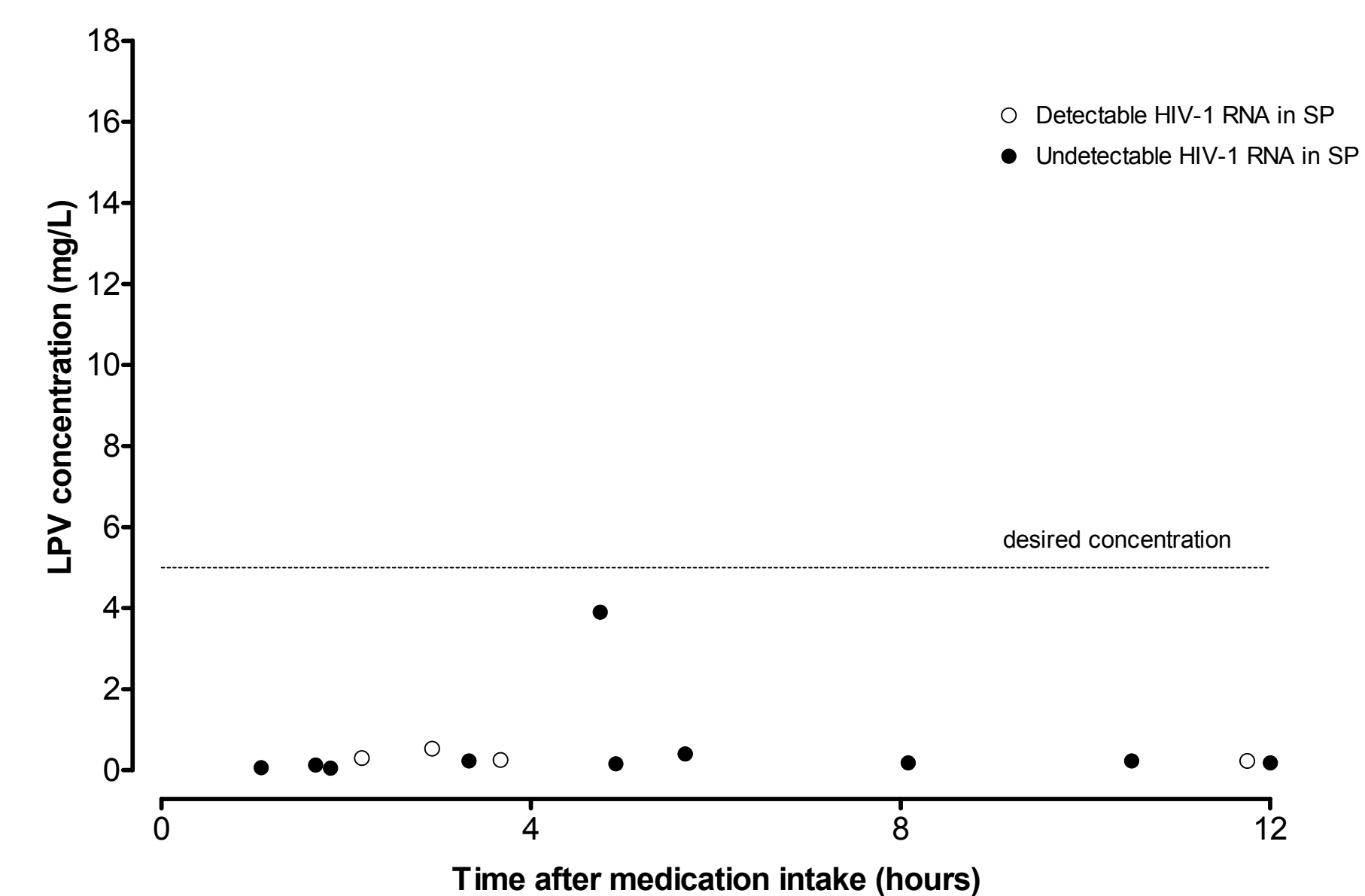
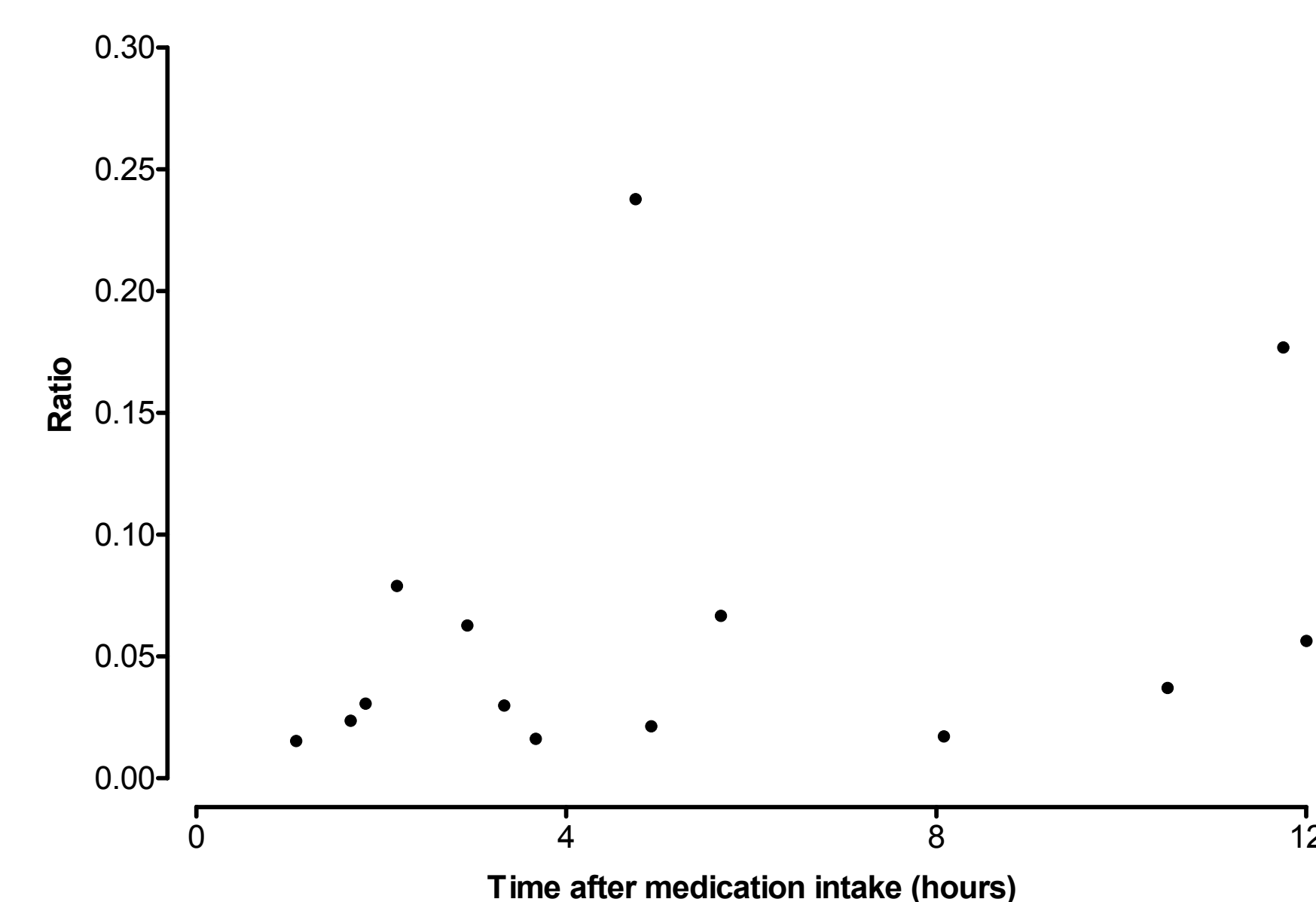


Figure 1c: Ratio of the concentrations of LPV in SP and in BP



Results

HIV RNA in BP and SP

- Nine patients started LPV because of virological failure. Four of them had detectable HIV-1 RNA in BP and 3 of these 4 patients had detectable HIV-1 RNA in SP at the time the samples were taken.
- Five patients started LPV because of side effects of their previous regimen. All had undetectable HIV-1 RNA in BP and in SP.

LPV concentrations in BP and SP

- LPV concentration in BP were below the desired concentration of 5.0 mg/L in 5 patients and above 5 mg/L in 9 patients.
- LPV concentration in SP ranged between 0.046 and 3.9 mg/L (median 0.23 mg/L, IQR 0.15-0.33).
- There was no relation between the LPV concentration in SP and the time since medication intake ($\rho = 0.22$, $p=0.45$; Spearman's rank).
- There was a weak relation between the BP concentration and the SP concentration ($\rho = 0.51$, $p=0.07$; Spearman's rank).
- The median ratio of the concentrations of LPV in SP and in BP was only 0.034 (IQR 0.021-0.070).

Conclusions

LPV has a poor penetration into SP. Although most of the patients had an undetectable HIV-1 RNA in SP, the median time on LPV was only 16 weeks. A longer follow-up is needed to determine whether these suboptimal concentrations in SP lead to a selection of resistant HIV-1 strains in BP and in SP.

Acknowledgment

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