

15th International HIV Drug Resistance Workshop



13-17 June 2006, Sitges, Spain

REPLICATION CAPACITY AND DRUG SUSCEPTIBILITY OF LOPINAVIR-RESISTANT HIV-2

Antivir Ther. 2006, 11:S49 (abstract no. 41)

H Mo¹, X Lu², S Masse¹, T Dekhtyar¹, L Lu¹, R Mondal¹, G Koev¹, T Ng, B Bernstein¹, F Gao² and A Molla¹

¹Abbott Laboratories, Abbott Park, IL; ²Duke University Medical Center, Durham, NC, USA

BACKGROUND: Lopinavir/ritonavir (LPV/r) has demonstrated durable antiviral activity in HIV-1 infected antiretroviral-naïve and protease inhibitor (PI)-experienced patients. Limited case reports have suggested antiviral activity of LPV against HIV-2. Several case reports describe failure of LPV in HIV-2 infected patients in association with a single mutation of 47V to 47A. Information on LPV activity against HIV-2, patterns of HIV-2 resistance mutations to LPV, or cross-resistance to other PIs of HIV-2 isolates with reduced LPV sensitivity is limited.

METHODS: The antiviral activities against HIV-2 strains and HIV-1 pNL4-3 were determined by either the standard MT-4/MTT assay or PBMC/RT assays. HIV-2 variants resistant to LPV were selected by passaging the HIV-2 virus in the presence of increasing concentrations of LPV (up to 1 µM). The protease-coding region was sequenced by the automatic sequencer ABI-3130XL. HIV-2 mutant molecular clones were generated by site-directed mutagenesis.

RESULTS: LPV demonstrated similar activity to that observed against HIV-1 virus in two strains of HIV-2 with IC₅₀ values of 0.012 µM in CBL 23 and 0.015 µM in MS, compared with 0.018 µM in HIV-1 pNL4-3. However, an approximately 10-fold reduction in LPV activity was observed in HIV-2 strain CDC 310319. Passage of HIV-2 MS strain with incrementally increasing concentrations of LPV selected mutations V47A and D17N in protease. Introduction of both 17N and 47A either individually or together into HIV-2 ROD, a molecular infectious clone, showed that single mutant V47A and double mutant G17N/V47A mutants exhibited an approximately 10-fold reduction in susceptibility to LPV. The single G17N mutant retained full LPV susceptibility. In contrast, TMC-114 demonstrated activity similar to wild-type HIV-2 against both V47A

and G17N/V47A. Saquinavir (SQV) was approximately 15-fold more active against both V47A and G17N/V47A mutants compared to wild-type HIV-2. Both V47A and G17N/V47A mutants grew approximately 30% slower than wild-type HIV-2.

CONCLUSIONS: LPV/r may provide antiviral activity in HIV-2 infected patients. However, the emergence of a single mutation at I47A may be associated with significantly reduced LPV activity against HIV-2. However, these isolates may maintain susceptibility to TMC-114 and be hyper-susceptible to SQV.

2006-06-13

41

Copyright © 2006 - [International Medical Press Ltd.](#) Reproduction of this abstract (other than one copy for personal reference) must be cleared through the International Medical Press Ltd. 2-4 Idol Lane, London EC3R 5DD UK.