Nouhin et al. BMC Proceedings 2011, 5(Suppl 1):P89
http://www.biomedcentral.com/1753-6561/5/S1/P89

BMC Proceedings

POSTER PRESENTATION Open Access

HIV drug resistance profile of HIV-1 CRF 01_AE protease and integrase coding regions in HIV infected Cambodian patients failing LPV-based 2nd line antiretroviral regimen

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From Institut Pasteur International Network Annual Scientific Meeting
Hong Kong. 22-23 November 2010

Background

By the end of 2009, the number of HIV-1 infected patients on RTI-based 1st line and PI-based 2nd line ARV regimen in Cambodia reached 34,000 and 1,500, respectively. We already reported good virological and immunological responses after 1 to 4 years in cohorts of patients on 1st line and more recently, among an Esther cohort of 70 patients after 2 years on LPVr-based 2nd line regimen. However, emergence of LPV resistant associated mutations is becoming a major concern in low and middle income countries.

Objective

This study aimed to describe the resistance pattern of both the protease (PR) and integrase (IN) coding regions in HIV-1 CRF01-AE infected patients failing LPV-based 2nd line regimen in Cambodia.

Methods

Analysis of the Protease and Integrase drug resistance genotyping of 95 HIV-1 strains infected patients presenting detectable viral load on LPV/r-based 2nd line regimen in Cambodia.

Results

Lack of amplification in PR gene was observed for 18/95 presenting low viral load (median VL: 2.9Log_{10} copies/ml [IQR: 2.8-3.4]). The 77 other CRF01_AE strains, harbored polymorphism mutation in position M36, H69 and L89 conferring possibly resistance to TPV/r. Forty-nine (median VL: 5Log_{10} copies/ml [IQR: 4 - 5.5]) did not present any other PI associated resistance mutation. In contrast, 28 patients showed multiple resistances to PI. The median duration on LPV/r regimen was 34.5 months [IQR: 23.5 – 53.3] and the median VL was 5Log_{10} copies/ml [IQR: 4.3-5.6]. Twenty-five patients were resistant to LPV/r (7 possibly resistant). Twenty-seven were resistant to IDV, 21 and 19 to ATV/r and FPV/r, respectively. Twenty-five were resistant to NFV (10 possibly), 22 resistant to SQV/r (9 possibly). Seven showed resistance to DRV/r (5 possibly). Finally, excluding possible resistance, 21/28 (75%) was resistant for at least 3 PIs. Clinical investigation revealed that most of these 28 patients starting several RTIs and PIs early around 2000. All of them were sensitive to raltegravir, elvitegravir (integrase inhibitors), and etravirine (Non-Nucleoside reverse transcriptase inhibitorse).

Conclusion

This study indicates that 28/95 (29.5%) of Cambodian patients presenting detectable viral load on LPV/r–based 2nd line regimen developed resistance mutation for a large number of PIs. Most of them were not naïve for PI before LPV/r initiation. These results highlight an urgent need to evaluate the efficacy of LPV/r-based 2nd line regimen at the national levels, allowing to design of a next 3rd line ARV regiment in low and middle income countries.

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Published: 10 January 2011

doi:10.1186/1753-6561-5-S1-P89
Cite this article as: Nouhin *et al.*: HIV drug resistance profile of HIV-1 CRF 01_AE protease and integrase coding regions in HIV infected Cambodian patients failing LPV-based 2nd line antiretroviral regimen. *BMC Proceedings* 2011 **5**(Suppl 1):P89.