

# 15th International HIV Drug Resistance Workshop



13-17 June 2006, Sitges, Spain

## **VIROLOGICAL CHARACTERIZATION OF TREATMENT NAÏVE SUBJECTS FAILING AN APLAVIROC-BASED REGIMEN WITH EITHER LAMIVUDINE/ZIDOVUDINE OR LOPINAVIR/RITONAVIR**

*Antivir Ther.* 2006, 11:S26 (abstract no. 21)

KM Kitrinou, DM Irlbeck, CC LaBranche, HA Madsen and JF Demarest  
*GlaxoSmithKline, Research Triangle Park, NC, USA*

---

**OBJECTIVES:** The antiviral activity of aplaviroc (APL) administered in combination with two nucleoside analogues or a boosted protease inhibitor was evaluated in treatment naïve subjects. Although studies were stopped prematurely due to idiosyncratic hepatotoxicity, a small number of subjects met protocol-defined virological failure (VF) criteria. Susceptibility to study drugs and coreceptor tropism were evaluated to assess the reason(s) for VF.

**METHODS:** Treatment naïve HIV+ subjects harbouring R5-tropic virus ( $n=265$ ) received APL with either lamivudine/zidovudine (3TC/ZDV) (CCR102881) or ritonavir boosted lopinavir (LPV/r) (CCR100136). For CCR100136, a subset of individuals ( $n=19$ ) enrolled with dual/mixed-tropic virus at screen. VF was defined as  $<1 \log_{10}$  copies/ml decrease from baseline plasma HIV-1 RNA by Week 4, or confirmed  $\geq 400$  after  $<400$  copies/ml HIV-1 RNA, or confirmed  $>0.5 \log_{10}$  copies/ml increase from the lowest HIV-1 RNA value. Plasma from baseline and VF were tested at Monogram Biosciences for HIV coreceptor tropism and APL susceptibility using the PhenoSense HIV Entry Assay (population and clones), and for RT/PR genotype/phenotype using the PhenoSenseGT Assay.

**RESULTS:** Eight subjects receiving APL/3TC/ZDV met VF criteria. The majority (6/8) acquired M184V and none had evidence of reduced susceptibility to APL. Nine subjects receiving APL/LPV/r met VF criteria with no evidence of treatment-emergent resistance to LPV/r or APL. However, five of these nine subjects harboured a minority of clones at baseline and/or VF with elevated APL  $IC_{50}$  values. Four VFs (two from each study) exhibited a change in population tropism readout from R5 to dual/mixed-tropic. Preliminary phylogenetic analyses of envelope clones suggest that changes in population

tropism readouts resulted from an increased proportion of pre-existing X4-using virus in the sampled population.

**CONCLUSIONS:** M184V was the only detected resistance mutation associated with VF in subjects receiving APL/3TC/ZDV. For VFs receiving APL/LPV/r, a minority of viruses in the quasispecies of 5/9 subjects showed reduced susceptibility to APL. Changes in population tropism readouts were relatively infrequent; additional data show that such changes may occur in the absence of treatment and/or during the initial viral load decline. Overall, very few subjects receiving an APL-containing regimen experienced VF. The pathway to resistance for APL remains to be determined.

2006-06-13

21

---

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.