

# 17th International HIV Drug Resistance Workshop



10-14 June 2008, Sitges, Spain

## Biological and clinical cut-off analyses for etravirine in the PhenoSense™ HIV assay

*Antivir Ther.* 2008; 13(Suppl. 3):A134 (abstract no. 122)

E Coakley<sup>1</sup>, C Chappey<sup>1</sup>, J Benhamida<sup>1</sup>, G Picchio<sup>2</sup>, L Tambuyzer<sup>3</sup>, J Vingerhoets<sup>3</sup> and M-P de Béthune<sup>3</sup>

<sup>1</sup>Monogram Biosciences Inc., South San Francisco, CA USA; <sup>2</sup>Tibotec Inc, Yardley, PA, USA; <sup>3</sup>Tibotec, Mechelen, Belgium

---

**BACKGROUND:** The DUET-1 and DUET-2 trials demonstrated the efficacy of etravirine in combination with darunavir/ritonavir in treatment-experienced patients. We explored the lower and upper clinical cutoff (LCCO and UCCO) for etravirine by evaluating week 2, 4, 8 and 24 HIV-1 RNA outcomes from the DUET studies in relation to baseline etravirine fold change (FC).

**METHODS:** Phenotyping and genotyping was performed on 199 baseline samples (PhenoSense HIV, Monogram Biosciences) from individuals whose optimized background therapy did not include enfuvirtide. The LCCO was defined as the FC above which HIV RNA response was first observed to decline relative to the reference population. The relative contribution of the background therapy was explored by deriving weighted, PhenoSense specific, continuous phenotypic susceptibility scores for new drugs in each regimen. Further exploratory analyses included linear regression and local linear fitting by the function lowess in subsets of the study population. The biological cut-off was defined as the 99th percentile of etravirine FC values from 1,693 viruses lacking known non-nucleoside reverse transcriptase inhibitor (NNRTI)-, nucleoside reverse transcriptase inhibitor- or protease inhibitor-selected mutations.

**RESULTS:** The etravirine biological cut-off was 2.9. Among the DUET samples the median (range) etravirine FC was 0.75 (0.06–200). Etravirine hyper-susceptibility (HS; FC<0.4) was observed in 67 samples (33.7%). Only 23 (11.5%) samples had both reduced darunavir (FC>10) and etravirine (FC>2.9) susceptibility. At entry only 13% of individuals were on efavirenz, nevirapine or delavirdine but 73% of samples had NNRTI mutations. A modest relationship was observed between etravirine FC and week 4 HIV RNA change in distributions unadjusted for the activity of background (R<sup>2</sup>=0.05, P=0.02). In models adjusted for the activity of background therapy the activity of etravirine was observed to be reduced at FC>2.9. This finding was supported by regression analyses in samples with reduced susceptibility to darunavir. Etravirine UCCO analyses were limited by the discrete number of

samples with higher etravirine FC and these analyses are ongoing.

**CONCLUSIONS:** In models accounting for the activity of background therapy a LCCO for etravirine was observed at FC 2.9. In this highly treatment experienced population etravirine HS was common, being observed in approximately one third of samples.

2008-06-10

122

---

Copyright © 2008 - [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.