

# 17th International HIV Drug Resistance Workshop



10-14 June 2008, Sitges, Spain

## HIV-1 GAG POLYMORPHISMS DETERMINE TREATMENT RESPONSE TO BEVIRIMAT (PA-457)

*Antivir Ther.* 2008; 13(Suppl. 3):A10 (abstract no. 8)

S McCallister<sup>1</sup>, J Lalezari<sup>2</sup>, G Richmond<sup>3</sup>, M Thompson<sup>4</sup>, R Harrigan<sup>5</sup>, D Martin<sup>6</sup>, K Salzwedel<sup>6</sup> and G Allaway<sup>6</sup>

<sup>1</sup>Panacos Pharmaceuticals, Watertown, MA, USA; <sup>2</sup>Quest Clinical Research, San Francisco, CA, USA; <sup>3</sup>Fort Lauderdale, FL, USA; <sup>4</sup>AIDS Research Consortium of Atlanta, Atlanta, GA, USA; <sup>5</sup>BC Centre for Excellence in HIV/AIDS, Vancouver, Canada; <sup>6</sup>Panacos Pharmaceuticals, Gaithersburg, MD, USA

---

**BACKGROUND:** Bevirimat is a novel HIV-1 maturation inhibitor in Phase II development that targets the capsid SP-1 cleavage site of Gag. Despite optimal plasma concentrations, not all patients given bevirimat have a robust viral load reduction (VLR). The determinants of treatment response were unknown.

**METHODS:** In a study to assess the bevirimat trough level associated with an optimal treatment response, 44 heavily treatment-experienced patients were given bevirimat for 14 days as functional monotherapy in escalating dose groups. Baseline clinical and virological variables were assessed to establish the determinants of bevirimat response. Response was also correlated with a standard Gag amino acid sequence.

**RESULTS:** Nineteen of the 20 responder patients ( $\geq 0.5 \log_{10}$  VLR) and 19/24 non-responder patients ( $< 0.5 \log_{10}$  VLR) had optimal bevirimat trough levels of at least 20  $\mu\text{g/ml}$ . In this bimodal bevirimat treatment response distribution, the mean VLR was -1.26 or -0.05  $\log_{10}$  copies/ml for responder or non-responder patients, respectively. Non-responder patients had more frequent baseline Gag polymorphisms near the capsid SP-1 cleavage site than responders (7.3; 5.9; P=not significant); Q369H, V370A and T371A/T371 deletion were more frequent in non-responders. Patients with any amino acid change at positions 369, 370 and 371 had mean VLR of -0.16, -0.24 and -0.32  $\log_{10}$ , respectively. Patients with consensus amino acid at 369, 370 and 371 had mean VLR of -0.69, -0.79 and -0.73  $\log_{10}$ , respectively. Patients without any change at 369, 370 or 371 had mean VLR of -1.08  $\log_{10}$ . Twelve (92%) of the 13

patients with bevirimat trough  $>20$   $\mu\text{g/ml}$  and with consensus amino acid at 369, 370 or 371 had VLR  $>0.5 \log_{10}$ . Lower baseline CD4+ T-cell count was the only clinical variable significantly ( $P=0.01$ ) associated with non-response. Analysis of Gag genotype in a separate database of 567 treatment-naïve HIV positive patients showed that 60.2% had the clade B consensus amino acid at positions 369, 370 or 371.

**CONCLUSIONS:** Using a genotype assay, treatment response to bevirimat is associated with baseline amino acid polymorphisms at Gag positions 369, 370 or 371 on SP-1; lower baseline CD4+ T-cell count may be a surrogate for these Gag changes. The Gag data were confirmed by phenotypic assay and a new prospective clinical study to verify these findings is underway.

2008-06-10

8

---

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.