

14th International HIV Drug Resistance Workshop



7-11 June 2005, Québec City, Canada

FDA ANALYSIS OF THE EFFECT OF BASELINE PROTEASE GENOTYPE ON VIROLOGICAL RESPONSE TO ATV/RTV VS LPV/RTV IN THE TREATMENT-EXPERIENCED SUBJECTS IN STUDY AI424045

Antivir Ther. 10, Suppl 1:S31 (abstract no. 29)

K Struble and [LK Naeger](#)✉

Division of Antiviral Drug Products, Center for New Drug Evaluation, Food and Drug Administration, Rockville, MD, USA

BACKGROUND: Resistance testing is important in clinical trials to determine the effect of an antiviral drug on the evolution of the virus and to identify the baseline genotypic and phenotypic determinants of virological success or failure. The Division of Antiviral Drug Products at the FDA undertakes several types of resistance analyses during the review of new drugs to characterize an anti-HIV drug's resistance profile by examining the development of HIV mutations on treatment, baseline genotype/phenotype and virological response, and cross-resistance. Baseline genotype and virological response analyses help assess the association between a specific mutation or mutational pattern and virological response rates, thus providing valuable information for physicians and HIV patients for optimal use.

METHODS: We performed resistance analyses of Study AI424045, sponsored by Bristol-Myers Squibb. This study evaluated the safety and efficacy of atazanavir/ritonavir (ATV/RTV) compared to lopinavir/ritonavir (LPV/RTV) in treatment-experienced subjects. Our analyses evaluated HIV-1 RNA response for ATV/RTV or LPV/RTV based on the presence and absence of baseline primary PI mutations. Virological response was defined as the proportion of subjects achieving <400 copies/mL HIV-1 RNA by the Roche Amplicor HIV-1 Monitor Assay. Genotypic analyses were performed by LabCorp, Inc.

RESULTS AND CONCLUSION: Both the number and type of baseline PI mutations affected response rates in treatment-experienced subjects. Genotypic analysis of baseline isolates showed that the presence of mutations M46I/V/L, I54V/L/M/A/T, A71V/T/I, V82A/T/F/S, I84V, or L90M at baseline reduced response rates in both the ATV/RTV and LPV/RTV treatment arms. Response rates were similar (63–65%) between

ATV/RTV and LPV/RTV-treated subjects with zero to four PI-associated mutations at baseline. Response rates were reduced for both treatments if five or more PI-associated mutations were present at baseline; 0% (0/9) for ATV/RTV compared to 28% (5/18) for LPV/RTV. Analysis by both number and type of baseline primary PI mutation showed ATV/RTV response rates were reduced to <30% if three or more primary PI mutations including changes at M36, M46, G73, V82, I84, or L90 were present at baseline. LPV/RTV response rates were reduced to <30% if three or more primary PI mutations including changes at M46 or V82 were present at baseline.

PRESENTING AUTHOR: LK Naeger

2005-06-07
29

Copyright © 2005 - [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.