Journal of the International AIDS Society

Poster presentation

Pharmacokinetic interactions between buprenorphine/naloxone and tipranavir/ritonavir in HIV-negative subjects chronically receiving buprenorphine/naloxone

RD Bruce*[1], FL Altice[1], DE Moody[2], S Lin[2], WB Fang[2], JP Sabo[3], JM Wruck[3], C Conner[3], P Piliero[3], L Andrews[1] and GH Friedland[1]

Address: [1]Yale University, New Haven, USA, [2]Center for Human Toxicology, University of Utah, Salt Lake City, USA and [3]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, USA

* Corresponding author

from Ninth International Congress on Drug Therapy in HIV Infection
Glasgow, UK. 9–13 November 2008

Published: 10 November 2008

Journal of the International AIDS Society 2008, **11**(Suppl 1):P240 doi:10.1186/1758-2652-11-S1-P240

This abstract is available from: http://www.jiasociety.org/content/11/S1/P240

Purpose of the study

Pharmacokinetic and pharmacodynamic interactions between antiretroviral and substance abuse therapies can adversely influence efficacy and toxicity of either or both agents. The primary objective of this study was to assess the effect of steady-state tipranavir 500 mg co-administered with ritonavir 200 mg (TPV/r) twice daily on the steady-state pharmacokinetics of buprenorphine/naloxone (BUP/NAL) in subjects chronically treated with BUP/NAL.

Methods

This was a multiple dose, open-label, sequential, non-randomized study in HIV-negative subjects stabilized on at least 3 weeks of BUP/NAL therapy.

Summary of results

At day 7 of concomitant administration, buprenorphine AUC and Cp24 h were not affected by co-administered TPV/r (<6% change relative to BUP/NAL alone) while Cmax decreased approximately 14%. Norbuprenorphine, the major BUP metabolite, AUC, Cmax and Cp24 h were decreased approximately 80% when co-administered with TPV/r. NAL AUC and Cmax were decreased approximately 44% and 36%, respectively, when coadministered with TPV/r. The last measurable plasma NAL concentration (Clast) in the concentration-time profile was decreased by 20%. Despite these pharmacokinetic effects, there was no clinical evidence of opioid withdrawal as measured by the Objective Opiate Withdrawal Scale and the Subjective Opiate Withdrawal Scale, and no need to modify buprenorphine dose. Because the study design did not include treatment with tipranavir and ritonavir alone, comparison was made to data from historical controls. TPV Cmax was unchanged (~6% decrease) while AUC and Cp12 h decreased 26% and 39%, respectively. Ritonavir concentrations at or near the end of the 12-h TPV/r dosing interval (Clast) were similar to historical controls, but ritonavir geometric mean Cmax and AUC were lower in the present study by 40–50% and 35%, respectively.

Conclusion

The results of this study indicate that no dosage modification of buprenorphine/naloxone is required when it is co-administered with TPV/r. The mechanism by which BUP/NAL affected the pharmacokinetic parameters of TPV is unclear; however, it is likely that the effect of lower plasma RTV exposure contributed substantially to the effect on tipranavir. Caution should be used when combining BUP/NAL with TPV/r as tipranavir may be less effective due to decreased tipranavir plasma concentrations in patients taking these agents concomitantly.