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THE EFFECT OF MULTIPLE DOSE ATORVASTATIN ON THE SINGLE-DOSE PHARMACOKINETICS OF COLCHICINE ADMINISTERED TO HEALTHY ADULT SUBJECTS AS A SINGLE 0.6-MG DOSE UNDER FASTED CONDITIONS

ACC Poster Contributions
Ernest N. Morial Convention Center, Hall F
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Session Title: Unique Trends in Hyperlipidemia
Abstract Category: 15. Pharmacology/Hormones/Lipids–Clinical
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Background: Gout affects more than 5 million adults in the US, and the prevalence is increasing. The average gout sufferer has multiple comorbidities such as metabolic syndrome and cardiovascular disease which also require medications, increasing the potential for adverse drug reactions and drug-drug interactions (DDIs). Atorvastatin is widely prescribed for the treatment of hyperlipidemia. COLCRYS® (colchicine USP, Mutual), is the only FDA-approved colchicine (COL) for the treatment and prevention of gout flares. Both atorvastatin and COL are metabolized by cytochrome P450 3A4 (CYP3A4) and are substrates of P-glycoprotein (P-gp). The potential for significant COL DDIs results from the interaction with agents that inhibit P-gp and CYP3A4. In several studies by Mutual, total COL exposure increased ~12 to 200% (on the basis of maximal concentration [Cmax]) and 40 to 240% (on the basis of area under the curve [AUC]) when given with several known P-gp and CYP3A4 inhibitors. This Phase 1 DDI study was conducted to determine the effect of multiple-dose atorvastatin on the pharmacokinetics (PK) of COL

Methods: Healthy volunteers (N = 24) received COL 0.6 mg on Day 1and and then completed a 14-day washout period. Beginning on the morning of Day 15, subjects received 40-mg of atorvastatin once daily on a non-confined basis for a total of 14 doses. On Day 28, subjects received COL 0.6-mg coadministered with 40-mg dose of atorvastatin on a confined basis. Serial blood samples for PK analysis were collected predose and postdose administration on Days 1 and 28 up to 24 hours postdose.

Results: When co-administered with steady-state atorvastatin, COL mean concentrations (Cmax and AUC0-t) increased approximately 31% and 27%, respectively. Seventeen (17) adverse events (AEs) were reported by 7 subjects (29%). The most common AEs were headache (13%) and dizziness (9%); all AEs were mild to moderate in severity.

Conclusions: A significant DDI is present when COL and atorvastatin are co-administered; however, the clinical significance of the increases is unknown. Despite the increase in exposure to COL, there was no apparent difference in the AE profile when COL was given alone or with a steady-state regimen of atorvastatin.