Coadministered amlodipine plus atorvastatin is well tolerated in patients with concomitant HTN/DYS. Furthermore, AEs observed with coadministered amlodipine plus atorvastatin are similar in nature, severity, and frequency to those seen with amlodipine or atorvastatin alone.

Key Words: Antihypertensive Agents, Lipid-Lowering Therapies, Safety and Tolerability

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EFFICACY AND SAFETY OF SILDENAFIL CITRATE IN PULMONARY ARTERIAL HYPERTENSION (PAH): RESULTS OF A MULTINATIONAL, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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The purpose of this study was to evaluate the efficacy and safety of sildenafil, a phosphodiesterase 5 inhibitor, in patients with PAH.

In this double-blind, placebo-controlled study, 278 patients with PAH were randomized to oral placebo or sildenafil (20, 40, or 80 mg) 3 times daily. The primary endpoint was change in 6-minute walk distance from baseline to Week 12. Secondary endpoints were change from baseline in mean pulmonary artery pressure (MPAP), time from randomization to clinical worsening, and change from baseline in Borg dyspnea score.

The 6-minute walk distance increased in all sildenafil groups compared with placebo; mean placebo-corrected treatment effects were 45 m (99% confidence interval [CI], 21–70; P = 0.001), 46 m (99% CI, 20–72; P = 0.001), and 50 m (99% CI, 23–77; P = 0.001) for 20, 40, and 80 mg sildenafil 3 times daily, respectively. All sildenafil doses reduced MPAP at Week 12; mean placebo-corrected treatment effects were -2.7 mmHg (95% CI, -5.4 to -0.1; P = 0.021) for 20 mg, -3.0 mmHg (95% CI, -5.3 to -0.7; P = 0.006) for 40 mg, and -5.1 mmHg (95% CI, -7.5 to -2.6; P = 0.001) for 80 mg sildenafil. Compared with placebo, there were trends towards reductions in the incidence of clinical worsening events (in particular, hospitalizations) and improvement in the level of dyspnea during exercise in the sildenafil-treated groups. Adverse events were of mild to moderate severity, consistent with the natural history of PAH and the established safety profile of sildenafil administered for erectile dysfunction.

This study confirms the efficacy and safety of sildenafil in the treatment of patients with PAH.

Key Words: Exercise Tolerance, Pulmonary Arterial Hypertension, Sildenafil

P-244 MP-26

HEMODYNAMIC EFFECTS OF SILDENAFIL CITRATE IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION (PAH)

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Sildenafil inhibits phosphodiesterase 5, enhancing cGMP-mediated relaxation of vascular smooth muscle. We report the hemodynamic effects of chronic oral sildenafil therapy in patients with PAH.

This 12-week, double-blind, placebo-controlled study randomized 278 PAH patients to placebo or sildenafil (20, 40, or 80 mg) 3 times daily. Hemodynamic measurements, performed at trough plasma concentrations of study medication, were made at baseline and Week 12.

Sildenafil significantly decreased mean pulmonary artery pressure (MPAP) and pulmonary vascular resistance (PVR), and increased cardiac output (CO) and mixed venous oxygen saturation (MVO2) (Table).