## 12 Inhaled Salmeterol Induces Salivary Alpha Amylase Activity in Healthy Subjects

**Andrea A. Pappalardo, MD**[1,2], Sherlyana Surja, MD[3], Caitlin M. Campion[2], Sarah J. Aldrich[2], James N. Moy, MD[2,3]; [1]Asthma and Allergy Center, Bloomingdale, IL, [2]Rush University Medical Center, Chicago, IL, [3]John H. Stroger Hospital of Cook County, Chicago, IL.

**RATIONALE:** Salivary alpha-amylase (sAA) secretion is an indirect method of measuring beta-receptor activation. Increases in sAA are seen in isoproterenol-infused mice (attenuated by beta-receptor antagonists) and in humans under physical or mental stress. We previously demonstrated that albuterol given by inhalation increases sAA (peaking at 15 minutes) in healthy volunteers and patients with asthma. We hypothesized that inhaled salmeterol, but not the anticholinergic ipratropium, will induce sAA secretion.

**METHODS:** Five healthy volunteers were enrolled. Spirometry was performed; and sAA, blood pressure and heart rate were collected at baseline and at 15, 30, 60 and 120 minutes after inhalation of fluticasone-salmeterol HFA (90 mcg/42 mcg). Two weeks later, two of the subjects repeated the protocol after inhaling ipratropium (34 mcg). Three additional subjects performed spirometry maneuvers alone to confirm stability of sAA during forced expiratory maneuvers.

**RESULTS:** Baseline sAA was 143±51 (U/mL±SEM) , which increased after salmeterol inhalation to 190±57, 230±68, 276±100, and 239±70 at 15, 30, 60, and 120 minutes, respectively; peaking at 60 minutes ($p<0.05$ at 60 and 120 minutes; ANOVA). sAA did not change after ipratropium inhalation or spirometry alone. $FEV_1$ did not change from baseline after inhalation of salmeterol or ipratropium in these healthy volunteers. No significant changes in blood pressure and heart rate were observed in any group.

**CONCLUSIONS:** Salmeterol induces sAA in healthy subjects, but peaks later than albuterol, consistent with its pharmacokinetic properties. These findings reinforce the concept that sAA is a surrogate marker for beta-2-receptor activation and may be useful in assessing tachyphylaxis or unresponsiveness to beta-2-agonists.

## 13 A New Look at an Old Drug

**Ronald A. Strauss, MD**; Case Western Reserve University School of Medicine, Fairview Park, OH.

**RATIONALE:** To study the efficacy of subcutaneous terbutaline in asthmatics who already have used inhaled beta agonists 3-10 times prior to their visit and to survey physician use of subcutaneous terbutaline in asthmatics who have an exacerbation.

**METHODS:** The asthmatics enrolled in this study were on daily medications including an inhaled steroid LABA combination. In addition, they used a beta agonist by inhalation at least three times as well as oral corticosteroids during the previous 24 hours. Twenty seven patients met these requirements. They were treated with subcutaneous terbutaline and an albuterol aerosol.The survey asked physicians to respond anonymously to the following: If a patient presents with an exacerbation of asthma you: ALWAYS, SOMETIMES, RARELY, or NEVER use subcutaneous terbutaline.

**RESULTS:** Twenty seven patients responded, at times dramatically to terbutaline, followed by an albuterol aerosol; with the addition of prednisone the symptoms resolved within 3-14 days. After the subcutaneous terbutaline and an albuterol aerosol, pulmonary function tests revealed an average increase in the FVC of 9%, $FEV_1$ of 7 %, $FEF_{25-75\%}$of 4%, and Peak Flow of 11%. Two patients (7%) required hospitalization. The survey was sent to 838 physicians; 372 responded (44%). 0% ALWAYS, 2% SOMETIMES, 12% RARELY, and 88% NEVER use subcutaneous terbutaline.

**CONCLUSIONS:** Subcutaneous terbutaline is clearly efficacious for those who have not responded to multiple beta agonist treatments. Subcutaneous terbutaline should be considered in patients who are receiving maximum pharmacological therapy.

## 14 Effects of Doubling the Highest Indicated Dose of Budesonide/Formoterol (BUD/FM) on Lung Function and Symptoms in Moderate-to-Severe Asthma with Fixed Airflow Obstruction (FAO)

**Michael DePietro, MD**[1], Donald P. Tashkin, MD[2], Bradley E. Chipps, MD, FAAAAI[3], Frank Trudo, MD[1]; [1]AstraZeneca LP, Wilmington, DE, [2]David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, [3]Capital Allergy & Respiratory Disease Center, Sacramento, CA.

**RATIONALE:** To assess whether doubling the highest indicated BUD/FM dose additionally benefits lung function and symptoms in moderate-to-severe asthmatic patients with FAO.

**METHODS:** A 52-week study randomized patients ≥12 years 3:1:1 to bid BUD/FM 640/18μg, BUD/FM 320/9μg, or BUD 640μg via pMDI. (NCT00651768). Post-hoc FAO status was assessed via screening post-bronchodilator $FEV_1/FVC < LLN$ (FAO+) or ≥LLN (FAO−) (described in *J Asthma* 2014;51(6):603–609). Findings are reported for BUD/FM mean changes from baseline in specified lung function and asthma control outcomes.

**RESULTS:** BUD/FM 640/18μg (n=209) versus 320/9μg (n=50) showed similar changes in $FEV_1$ in FAO+ and FAO− patients (0.22 vs 0.19 L and 0.17 vs 0.18 L, respectively), and in % responders with $FEV_1$≥100 mL (63.9% vs 72.7% and 63.5% vs 65.4%, respectively). BUD/FM 640/18μg versus 320/9μg showed similar changes in morning PEF in FAO+ (37.9 vs 36.7 L/min) but numerically higher changes in FAO− (43.7 vs 30.9 L/min) patients. Percentages of responders with morning PEF ≥30 L/min were numerically lower with 640/18μg vs 320/9μg in FAO+ (54.2% vs 59.1%) and higher in FAO− (59.5% vs 50.0%) patients. BUD/FM 640/18μg versus 320/9μg showed similar changes in % asthma control days (ACDs) (days without symptoms or rescue medication use) in FAO+ and FAO− (30.3% vs 31.3% and 21.5% vs 24.4%) and in % of patients who experienced a ≥10% increase in ACDs in FAO+ and FAO− (65.1% vs 68.2% and 54.8% vs 57.7%).

**CONCLUSIONS:** Post-hoc, no additional benefit was seen with BUD/FM 640/18μg vs BUD/FM 320/9μg in FAO+ moderate-to-severe asthma patients.

Supported by AstraZeneca.