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## **“Placebo-Controlled Study of Oral Montelukast in the Acute Management of Children with Moderate Asthma Exacerbations”**

A study proposal

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### **ABSTRACT**

**OBJECTIVE:** To investigate the short-term effectiveness of montelukast (added to standard acute asthma therapy) to improve airway function measured by forced expiratory volume in one second (FEV<sub>1</sub>) in children with acute moderate asthma exacerbations.

**METHODS:** In a randomized blinded placebo-controlled design, a convenience sample of children age 6 to 14 years old was enrolled upon presentation to our urban pediatric emergency department (ED) for evaluation and treatment. Subjects received either montelukast 5-milligrams or matching placebo by mouth in addition to standard emergency asthma care which consisted of inhaled bronchodilators (albuterol and ipratropium bromide) and oral steroids (prednisolone or prednisone). The primary outcome was the mean group change (improvement) in FEV<sub>1</sub> (%predicted) after three hours. FEV<sub>1</sub> was measured prior to administration of study medication and initial therapy and at three 60-minute intervals. Hospitalization rates for each group were measured as a secondary outcome. Three days after the ED visit, subjects' parents were telephoned to evaluate other secondary outcomes.

**RESULTS:** 11 subjects in the Montelukast group and 12 subjects in the Placebo group completed the final FEV<sub>1</sub> measurement. Baseline characteristics were similar between groups except for age (Montelukast group  $\mu=9.8 \pm 2.4$  years; Control group  $\mu=11.9 \pm 2.7$  years), gender (female:male ratio = 2:11 for Montelukast group; 5:9 for Control group), and initial peak expiratory flow rate (% predicted; Montelukast group  $\mu=49.4 \pm 5.6$ ; Control group  $\mu=55.5 \pm 6.4$ ). Both groups had significant mean improvement in FEV<sub>1</sub> after three hours (Montelukast group  $\mu=16.8\% \pm 11.4$ ,  $p<0.001$ ; Control group  $\mu=19.9\% \pm 12.1$ ,  $p<0.001$ ; paired t-test). While the Control group had a greater mean improvement after three hours, there was no statistical difference in improvement between groups ( $p=0.56$ , Wilcoxon 2-sample test). The conditional power was 39% from this interim analysis. The probability that the study Montelukast group ( $\mu=16.8\%$ ) could be randomly sampled from a theoretical distribution with  $\mu=32-35\%$  (the hypothesized 12% greater mean improvement for Montelukast group compared to Control group) is near zero. In order for the Montelukast group to have a mean improvement  $>31\%$ , at least twenty future enrolled subjects would need individual FEV<sub>1</sub> improvements  $>41\%$ . Only three subjects in both study groups had FEV<sub>1</sub> improvements  $>25\%$  (two were in the Control group). There were no statistical differences between groups in the secondary outcomes, and there were no increased rates of adverse events in the Montelukast group.

**CONCLUSIONS:** This interim analysis showed no further improvement in FEV<sub>1</sub> if montelukast was added to standard acute asthma therapy. Further analysis suggests that a significant difference between groups would be unlikely if the study were completed. In conclusion, montelukast given as 5-milligrams orally in addition to standard acute asthma therapy is unlikely to further improve FEV<sub>1</sub> after three hours.