who were managed by this algorithm, then 1 had an asthma exacerbation that was prevented.

Analysis of the individual types of exacerbations showed no difference in hospital admission or visits to an emergency department or labor ward. Patients in the control group had a significantly higher rate of unplanned or unscheduled clinic visits (p=0.002), and significantly more patients required oral steroids as compared with the F_ENO group (p=0.04). The algorithm was associated with a significantly lower daily dose requirement of inhaled corticosteroids (p=0.043).

"Asthma exacerbations during pregnancy can be significantly reduced by the use of a validated F_ENO-based treatment algorithm," said Prof. Gibson. "Future work should investigate the application of this algorithm in routine antenatal care and other settings."

TESRA Study Results

Results from the Treatment of Emphysema with a Selective Retinoid Agonist (TESRA; NCT00413205) study showed that emphysema patients had a mixed response to treatment with the retinoid agonist palovarotene. Treatment with palovarotene failed to meet the primary endpoint of improving lung function (FEV_1) in the overall analysis. However, the subset of patients with lower lobe emphysema had a significant reduction in the rate of decline in lung function.

A post hoc analysis in the lower lung suggested that palovarotene was associated with less worsening over time in most outcomes in patients with lower lung emphysema predominance. "These findings are very much post hoc and preliminary and require confirmation using a more detailed analysis of emphysema progression in different parts of the lung. However, the observations from this hypothesis-generating study do suggest that they need to be tested again but in a group of patients identified beforehand as having predominant lower lung emphysema," said Paul W. Jones, MD, PhD, St. George's University of London, London, United Kingdom.

TESRA was a Phase 2, double-blind, randomized, placebo-controlled, multicenter trial that involved investigators at 69 centers in 12 countries. Palovarotene is an oral retinoid agonist that is selective for the gamma receptor, which is thought to play a key role in alveolar formation. In preclinical models of emphysema, the drug reduced inflammation, promoted structural repair, and improved lung function.

TESRA involved ex-smokers who had computed tomography-documented emphysema, baseline postbronchodilator FEV_1 <70% of predicted, and baseline TL_{CO} <70% of predicted. They were randomized 2:1 to palovarotene 5 mg/day or placebo, both in addition to optimized therapy for chronic obstructive pulmonary disease (COPD). Treatment and follow-up continued for 2 years. The primary outcome was the change in FEV_1 after 2 years.

When the trial ended, patients in the palovarotene arm had a 4.5-ml improvement in FEV_1 compared with the placebo group, a difference that failed to achieve statistical significance (p=0.86).

Four regions of interest had been identified in the lungs: upper quartile, upper half, lower half, and lowest quartile. Patients in the placebo arm had greater loss of lung function in the lower half and lowest quartile, compared with the upper half and upper quartile. A post hoc analysis of these regions of interest showed that in patients who were treated with placebo, the change in FEV_1 in the lower half of the lung averaged -56.7 ml at 12 months and -124.4 ml at 24 months and -56.2 ml at 12 months and -174.7 ml at 24 months in the lower quartile. In contrast, the rate of loss of FEV_1 in patients who were treated with paloverotene was less: lower half -33.0 ml and -40.9 ml at 12 and 24 months; lowest quartile: -56.2 ml and -46.0 ml at 12 and 24 months. A similar response pattern emerged with respect to DL_{CO}, 6-minute walk distance, and quality of life.

In addition to optimal COPD therapy, in patients with lower lung emphysema, palovarotene significantly reduced the decline in DL_{CO} and FEV_1, which may be suggestive of a disease-modifying effect.

Multicenter International Lymphangioleiomyomatosis Efficacy and Safety of Sirolimus Trial

Lung function in lymphangioleiomyomatosis (LAM) stabilized and symptoms and quality-of-life (QoL) improved significantly during treatment with sirolimus, according to results of the Multicenter International LAM Efficacy of Sirolimus (MILES) Trial, reported Francis X. McCormack, MD, University of Cincinnati, Cincinnati, Ohio, USA, on behalf of the NIH Rare Lung Diseases Consortium.

FEV_1 increased by 1 ml in the sirolimus group compared with a 12-ml decrease with placebo (p<0.0001) over the course of the 1-year treatment period. Forced vital capacity