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Abstracts' Service

A Summary of the New GINA Strategy: A Roadmap to Asthma Control

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Over the past 20 years, the Global Initiative for Asthma (GINA) has regularly published and annually updated a global strategy for asthma management and prevention that has formed the basis for many national guidelines. However, uptake of existing guidelines is poor. A major revision of the GINA report was published in 2014, and updated in 2015, reflecting an evolving understanding of heterogeneous airways disease, a broader evidence base, increasing interest in targeted treatment, and evidence about effective implementation approaches. During development of the report, the clinical utility of recommendations and strategies for their practical implementation were considered in parallel with the scientific evidence.

This article provides a summary of key changes in the GINA report, and their rationale. The changes include a revised asthma definition; tools for assessing symptom control and risk factors for adverse outcomes; expanded indications for inhaled corticosteroid therapy; a framework for targeted treatment based on phenotype, modifiable risk factors, patient preference, and practical issues; optimisation of medication effectiveness by addressing inhaler technique and adherence; revised recommendations about written asthma action plans; diagnosis and initial treatment of the asthma-chronic obstructive pulmonary disease overlap syndrome; diagnosis in wheezing pre-school children; and updated strategies for adaptation and implementation of GINA recommendations.

Prognostic Value of Variables Derived from the Six-minute Walk Test in Patients with COPD: Results from the ECLIPSE Study

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In addition to the six-min walk distance (6 MWD), other six-min walk test (6 MWT) derived variables, such as mean walk-speed (6MWSpeed), 6-min walk-work (6 MWW), distance-saturation product (DSP), exercise-induced oxygen desaturation (EID), and unintended stops may be useful for the prediction of mortality and hospitalization in patients with chronic obstructive pulmonary disease (COPD). We studied the association between 6 MWT-derived variables and mortality as well as hospitalization in COPD patients and compared it with the BODE index.

A three-year prospective study (ECLIPSE) to evaluate the prognostic value of 6 MWT-derived variables in 2010 COPD patients. Cox's proportional-hazard regressions were performed to estimate 3-year mortality and hospitalization.

During the follow-up, 193 subjects died and 622 were hospitalized. An adjusted Cox's regression model of hazard ratio [HR] for impaired 6 MWT-derived variables was significant referring to: mortality (6 MWD $\leq$334 m [2.30], 6MWSpeed $\leq$0.9 m/sec [2.15], 6 MWW $\leq$20000 m kg [2.17], DSP $\leq$290 m% [2.70], EID $\leq$88% [1.75], unintended stops [1.99]; and hospitalization (6 MWW $\leq$27000 m kg [1.23], EID $\leq$88% [1.25], BODE index $\geq$3 points [1.40]; all $p \leq 0.05$).

The 6 MWT-derived variables have an additional predictive value of mortality in patients with COPD. The 6 MWW, EID and the BODE index refine the prognosis of hospitalization.

Air Current Applied to the Face Improves Exercise Performance in Patients with COPD

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Purpose. Improving dyspnea and exercise performance are goals of COPD therapy. We tested the hypothesis that air current applied to the face would lessen dyspnea and improve exercise performance in moderate-severe COPD patients.

Methods. We recruited 10 COPD patients (5 men, age 62 ± 6 years, FEV_1 0.93 ± 0.11 L (34 ± 3 % predicted), TLC 107 ± 6 %, RV 172 ± 18 %) naïve to the study hypothesis. Each patient was randomized in a crossover fashion to lower extremity ergometry at constant submaximal workload with a 12-diameter fan directed at the patients face or exposed leg. Each patients' studies were separated by at least 1 week. Inspiratory capacity and Borg dyspnea score were measured every 2 min and at maximal exercise.

Results. Total exercise time was longer when the fan was directed to the face (14.3 ± 12 vs. 9.4 ± 7.6 min, face vs. leg, respectively, $p = 0.03$). Inspiratory capacity tended to be greater with the fan directed to the face (1.4 (0.6-3.25) vs. 1.26 (0.56-2.89) L, $p = 0.06$). There was a reduction in dynamic hyperinflation, as reflected by higher IRV area in the fan on face group (553 ± 562 a.u. vs. 328 ± 319 a.u., $p = 0.047$). There was a significant improvement in the Borg dyspnea score at maximal exercise (5.0 (0-10) vs. 6.5 (0-10), $p = 0.03$), despite exercising for 34 % longer with the fan directed to the face.

Conclusions. Air current applied to the face improves exercise performance in COPD. Possible mechanisms include an alteration in breathing pattern that diminishes development of dynamic hyperinflation or to a change in perception of breathlessness.

Lung-Function Trajectories Leading to Chronic Obstructive Pulmonary Disease

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Background. Chronic obstructive pulmonary disease (COPD) is thought to result from an accelerated decline in forced expiratory volume in 1 second (FEV_1) over time. Yet it is possible that a normal decline in FEV_1 could also lead to COPD in persons whose maximally attained FEV_1 is less than population norms.

Methods. We stratified participants in three independent cohorts (the Framingham Offspring Cohort, the Copenhagen City Heart Study, and the Lovelace Smokers Cohort) according to lung function (FEV_1 ≥80% or <80% of the predicted value) at cohort inception (mean age of patients, approximately 40 years) and the presence or absence of COPD at the last study visit. We then determined the rate of decline in FEV_1 over time among the participants according to their FEV_1 at cohort inception and COPD status at study end.

Results. Among 657 persons who had an FEV_1 of less than 80% of the predicted value before 40 years of age, 174 (26%) had COPD after 22 years of observation, whereas among 2207 persons who had a baseline FEV_1 of at least 80% of the predicted value before 40 years of age, 158 (7%) had COPD after 22 years of observation (P<0.001). Approximately half the 332 persons with COPD at the end of the observation period had had a normal FEV_1 before 40 years of age and had a rapid decline in FEV_1 thereafter, with a mean (±SD) decline of 53±21 ml per year. The remaining half had had a low FEV_1 in early adulthood and a subsequent mean decline in FEV_1 of 27±18 ml per year (P<0.001), despite similar smoking exposure.

Conclusions. Our study suggests that low FEV_1 in early adulthood is important in the genesis of COPD and that accelerated decline in FEV_1 is not an obligate feature of COPD. (Funded by an unrestricted grant from GlaxoSmithKline and others.)

Efficacy and Safety of Umeclidinium Added to Fluticasone Furoate/Vilanterol in Chronic Obstructive Pulmonary Disease: Results of Two Randomized Studies

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Objective. The aim of these studies (NCT01957163; NCT02119286) was to evaluate the efficacy and safety of umeclidinium (UMEC 62.5 µg and 125 µg) added to fluticasone furoate/vilanterol (FF/VI, 100/25 µg) in chronic obstructive pulmonary disease (COPD).

Methods. These were 12-week, double-blind, placebo-controlled, parallel-group, multicenter studies. Eligible patients were randomized 1:1:1 to treatment with once-daily blinded UMEC 62.5 µg (delivering 55 µg), UMEC 125 µg (delivering 113 µg) or placebo (PBO) added to open-label FF/VI (delivering 92/22 µg; N = 1238 [intent-to-treat population]). The primary endpoint was trough forced expiratory volume in one second (FEV_1) on Day 85; the secondary endpoint was 0–6 h post-dose weighted mean (WM) FEV_1 at Day 84. Health-related quality of life was reported using St George's respiratory questionnaire (SGRQ). Adverse events (AEs) were also assessed.

Results. In both studies, trough FEV_1 was significantly improved with UMEC + FF/VI (62.5 µg and 125 µg) versus PBO + FF/VI (range: 0.111–0.128 L, all $p < 0.001$ [Day 85]), as was 0–6 h post-dose WM FEV_1 (range: 0.135–0.153 L, all $p < 0.001$ [Day 84]). SGRQ results were inconsistent, with statistically significant improvements with UMEC + FF/VI versus PBO + FF/VI in one study only and with UMEC 62.5 µg only (difference in SGRQ total score from baseline between treatments: −2.16, $p < 0.05$). Across all treatment groups, the overall incidences of AEs were similar (30–39%), as were cardiovascular AEs of special interest (<1–3%) and pneumonia AEs (0–1%).

Conclusion. Overall, the addition of UMEC to FF/VI therapy resulted in significant improvements in lung function compared with PBO + FF/VI in patients with COPD, with similar safety profiles, though SGRQ results were inconsistent.

Clinical Relevance. The results from these two studies demonstrate that the addition of umeclidinium (62.5 ìg and 125 µg) to FF/VI (100/25 µg) provides statistically significant and clinically meaningful improvements in lung function compared with placebo + FF/VI in patients with COPD. Statistically significant improvements in quality of life with UMEC + FF/VI versus placebo + FF/VI were reported in one study only. Safety profiles were consistent across all treatment groups in both studies. These studies support the use of triple therapy in COPD, providing physicians with an alternative treatment option.

Maintaining Gains Following Pulmonary Rehabilitation

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Purpose. Pulmonary rehabilitation (PR) is an accepted intervention for individuals with chronic obstructive pulmonary disease. Despite initial improvements following PR, many patients eventually return to baseline function or decline even further. The aim of this study is to look at long-term (>1 year) outcomes following PR.

Methods. This was a prospective cohort study of patients who had completed PR. Participants were invited for an assessment consisting of participant interviews and clinical assessments using standardised instruments.

Results. 129 patients between 2003 and 2012 completed rehabilitation and were eligible. 88 patients were included in the analysis. The mean time of the long-term assessment was 22 months following PR. The mean age was 71 years. Mean FEV1 was 46 %. There was a statistically significant ($p < 0.001$) increase in the incremental shuttle walk test distance of 29.0 m following PR but this gain was lost at the long-term reassessment. Chronic Respiratory Questionnaire (CRQ) scores showed a statistically significant ($p < 0.001$) increase in all four domains but only the domains of dyspnoea and fatigue remained statistically significant ($p < 0.001$, $p < 0.01$, respectively) at the long-term reassessment. Hospital Anxiety and Depression Scale scores reduced following rehabilitation but only the anxiety component was statistically significant ($p < 0.01$). These improvements persisted at the long-term reassessment but were not statistically significant.

Conclusions. This study confirms that many of the functional gains achieved in PR are lost in the longer term. Regular surveillance or monitoring of these patients post-PR is important to identify those requiring further intervention.

Cigarette Smoke Exposure and the Acute Respiratory Distress Syndrome

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Objective. The association between cigarette smoke exposure and the acute respiratory distress syndrome in patients with the most common acute respiratory distress syndrome risk factors of sepsis, pneumonia, and aspiration has not been well studied. The goal of this study was to test the association between biomarker-confirmed cigarette smoking and acute respiratory distress syndrome in a diverse cohort.

Design. Prospective cohort.

Setting. Tertiary care center.

Patients. Four hundred twenty-six critically ill patients with acute respiratory distress syndrome risk factors (excluding trauma and transfusion).

Interventions. None.

Measurements and Main Results. We obtained smoking histories and measured urine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (a biomarker of cigarette smoke exposure) on urine samples obtained at the time of study enrollment. The association between cigarette smoke exposure and acute respiratory distress syndrome differed based on acute respiratory distress syndrome risk factor ($p < 0.02$ for interaction). In patients with nonpulmonary sepsis as the primary acute respiratory distress syndrome risk factor (n = 212), 39% of those with acute respiratory distress syndrome were current smokers by history compared with 22% of those without acute respiratory distress syndrome (odds ratio, 2.28; 95% CI, 1.24–4.19; $p = 0.008$). Likewise, cigarette smoke exposure as measured by urine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol was significantly associated with acute respiratory distress syndrome in this group. The increased risk of acute respiratory distress syndrome in nonpulmonary sepsis was restricted to patients with 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol levels consistent with active smoking and was robust to adjustment for other acute respiratory distress syndrome predictors. Cigarette smoke exposure as measured by history or 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol was not associated with acute respiratory distress syndrome in patients with other risk factors (e.g., pneumonia and aspiration).

Conclusions. Cigarette smoking measured both by history and biomarker is associated with an increased risk of acute respiratory distress syndrome in patients with nonpulmonary sepsis. This finding has important implications for tobacco product regulation and for understanding the pathogenesis of acute respiratory distress syndrome.