What's New in COPD?

Key Learnings from the European Respiratory Society's Annual Congress, Barcelona 2010

Introduction

The 2010 Congress of the European Respiratory Society (ERS) took place in September in Barcelona, Spain. As part of the wide range of issues and topics in respiratory disease and lung health covered at this year's Congress, several educational sessions and research presentations were focused on chronic obstructive pulmonary disease (COPD).

This report summarizes some of the highlights of the COPD-related material presented at the ERS 2010 Congress. The material encompasses a broad range of themes, including pathophysiology, predictors of prognosis, classification systems, comorbidities, treatment and monitoring.

THEME 1: COPD Diagnosis

From a Canadian perspective, one of the most interesting pieces of research related to COPD diagnosis was presented as a poster at the 2010 Congress. Canadian researchers presented the results of a survey administered to Canadian family physicians to assess their comfort in diagnosing COPD, and to prospectively assess their COPD practice patterns.[1] The survey involved 166 Canadian family physicians, who recorded a total of 3,275 patient visits between May and July, 2009. As shown in Figure 1, a large proportion (43%) of the surveyed physicians indicated that they were somewhat to not at all comfortable in diagnosing COPD. In addition, 52% were somewhat to not at all comfortable differentiating between asthma and COPD. The researchers concluded that these findings suggest a need for greater physician awareness, education and competency in the diagnosis of COPD.

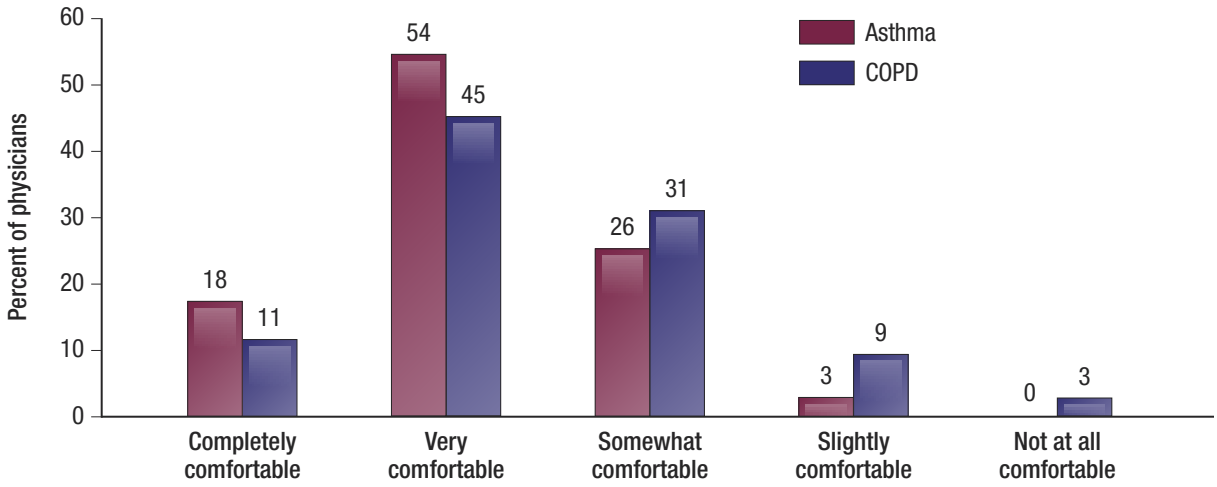
These findings may not be surprising, given some of the other discussions that took place at ERS 2010 regarding the differentiation between asthma and COPD. Even among experts in respiratory medicine, there is considerable debate as to whether these are, in fact, distinct clinical entities, two separate manifestations of similar underlying pathology, or some combination thereof. An entire symposium was dedicated to this question, with presentations from several leading experts in the field.[2-4] No consensus has yet been reached, but there is increasing evidence showing similarities in asthma- and COPD-related immunity and genetics and that the current categorization of patients to asthma or COPD based on clinical-trial findings does not reflect the reality of patient phenotypes. The patients enrolled in clinical trials, due to stringent inclusion and exclusion criteria, represent only an estimated 5% of COPD patients and 6% of asthma patients. As such, the ability to distinguish between the two entities using evidence-based medicine is problematic.

An Austrian study presented at ERS 2010 also shed some light on the diagnosis of COPD by primary-care physicians.[5] In this study, the investigators attempted to assess the feasibility of standardized spirometry in a random sample of primary-care offices. The response rate of these offices was only 50%. Of the 9,212 patients who attended the 30 responding offices, only 13% (1,230 patients) agreed to participate in spirometry. Of these patients, only 63% provided measurements in accordance with American Thoracic Society (ATS) criteria. The investigators concluded that, due to the low participation rate and low rate of spirometry meeting quality criteria, the primary-care office might not be appropriate for COPD case finding.

THEME 2: The Need for Better Reference Equations in Classification of COPD

A recurring theme at ERS 2010 was that there is a need for better reference equations for determining predicted lung function.[6-8] In a special symposium entitled "Unravelling the Natural History of Pulmonary Function and COPD," two presenters explained that existing reference equations are derived

FIGURE 1. **Comfort Level Diagnosing Asthma and COPD[1]**



from a limited pool of patients and have limitations for certain other populations, including the elderly, the very young and those of some ethnicities.[6,7] The need for better predictive equations is illustrated by the fact that there were five new equations presented at ERS 2010 alone.

The observations from this symposium were also supported by a poster presented by Canadian investigators at the Congress. Dr. Anthony D'Urzo et al attempted to describe how closely the decision logic of various spirometry interpretation algorithms conforms to guideline-defined spirometric diagnosis of asthma and COPD.[8] The algorithms were identified through a comprehensive literature search. The researchers observed considerable variation among the different algorithms and concluded that these variations could have important clinical implications, including disease misclassification.

> … a large proportion (43%) of [Canadian family] physicians surveyed indicated that they were somewhat to not at all comfortable in diagnosing COPD.

THEME 3: Predictors of Disease Course in COPD

A considerable amount of research presented at ERS 2010 dealt with predictors of disease course in COPD. Perhaps the most important of this research involved the three-year findings from the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) study.[9-11] Some of the study results were also published in the *New England Journal of Medicine* in September, 2010.[12]

ECLIPSE was a three-year, prospective, observational study conducted in 12 countries in Europe and North America. The objectives of the study were to define COPD subtypes, to define parameters that predict disease progression, to acquire data to correlate biomarkers and clinically relevant endpoints, and to identify novel genetic factors. The study enrolled a total of 2,164 COPD patients, aged 40-75 years, with a history of more than 10 pack-years smoking, FEV1 < 80% predicted, and FEV1:FVC ≤ 0.7 post bronchdilator. In addition, there were 337 controls who were smokers or ex-smokers and 245 controls who were never smokers.

The investigators reported that, although the mean Medical Research Council dyspnea scale, six-minute walk distance, St George's Hospital Respiratory Ques-

tionnaire for COPD patients (SGRQ-C) and exacerbation rate increased with increasing COPD severity (GOLD stage II to IV), they found that there was considerable variation for each outcome among individuals within a given GOLD stage. They therefore concluded that disease severity cannot be fully characterized using FEV alone.

With respect to disease phenotypes, the researchers studied frequent exacerbators (≥ 2 severe events/year), those who had rapid lung function (FEV1) decline (> 60 mL/year), those who were bronchodilator responders and those with COPD associated with systemic inflammation.

In the analysis of frequency of exacerbations, while associated with severity (Figure 2), the researchers reported that the best predictor, by far, was a prior exacerbation. The rate at which exacerbations occur reflects an independent susceptibility phenotype, which has implications for developing exacerbation-prevention strategies across the entire spectrum of disease severity.

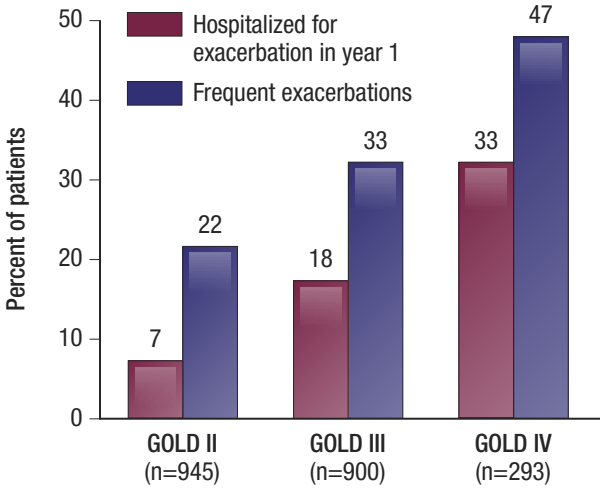
In terms of lung function decline, the ECLIPSE investigators reported that the rate of decline varied considerably in COPD subjects and that a significant proportion of subjects actually had improved lung function over three years. They did not identify any clinical characteristics that permitted detection of rapid decliners, including severity of COPD. They concluded that rate of FEV1 decline is a marker of disease activity, distinct from markers of disease severity.

The ECLIPSE study also showed that bronchodilator responders were not a useful phenotype, as those initially identified as responders became non-responders and vice-versa.

For systemic inflammation, the researchers analyzed 36 potential biomarkers from blood and sputum, including WBC, neutrophils, high-sensitivity C-reactive protein (hsCRP), IL-6, IL-8, fibrinogen and TNFα. In general, the levels of these biomarkers increased from non-smokers to smokers to COPD patients with increasing GOLD stage. However, once again, individuals within each group showed considerable variation independent of smoking status and disease severity. The researchers identified some biomarkers that were associated with occurrence of exacerbations: surfactant protein-D (SP-D), chemokine ligand-18 (CCL18/PAR C), fibrinogen and hsCRP.

Other research. In addition to ECLIPSE, much other research presented at ERS 2010 also looked into predictors of disease course and prognosis. Several studies, for example, attempted to identify predictors of mortality among patients admitted for an acute exacerbation of COPD. For example, a French study analyzed 1,142 such patients.[13] The investigators identified age, bronchiectasis, the number of admissions for COPD acute exacerbation in the 12 months preceding the recruitment admission, recent systemic treatment with corticosteroids, and long-term oxygen inhalation therapy as significant predictors of mortality.

FIGURE 2. **ECLIPSE Results: Association of Disease Severity with Frequency/Severity of Exacerbations in COPD[9]**

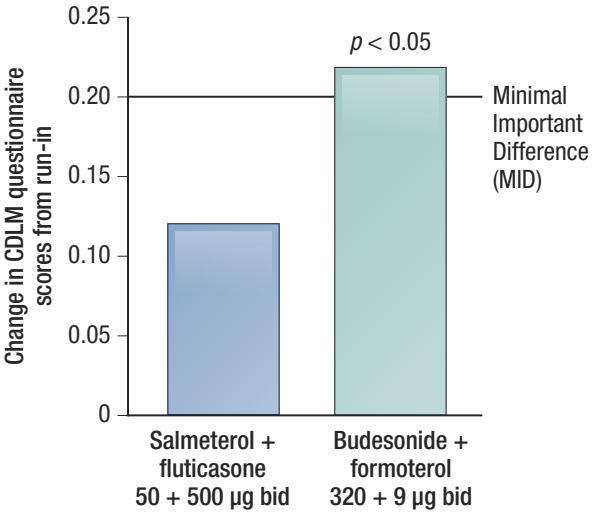


Frequency of exacerbations appears to be an independent phenotype with implications for management across all severities of disease.

A Belgian study of 145 patients hospitalized with an exacerbation of COPD showed that muscle weakness and the ADO index are significant predictors of prolonged hospital stay.[14]

A Spanish study involving 163 patients admitted for a COPD exacerbation (and who had not died during

FIGURE 3. **Improvement in Morning Activities (CDLM) with Budesonide + Formoterol[20]**



admission) showed that age, degree of baseline dyspnea, and number of admissions the previous year were all strong predictors of mortality.[15] The report showed that the risk of death within two years after discharge is doubled for each increase of level of dyspnea severity at the time of admission.

One of the factors identified in these studies, oxygen dependence, was examined in greater detail by a group of Swedish researchers.[16] Of note, they found that, while men and women with oxygen dependence were at significantly higher mortality risk, the relative risk was far higher for women than for men. For example, the standardized mortality ratio (SMR) for dying of COPD-related causes (relative to the general population) was 292.2 for women and 155.4 for men. For dying of heart failure (again, relative to the general population), the SMR was 9.2 for women and 4.1 for men. The SMR for death from all causes was 12.0 for women and 7.4 for men.

The [ECLIPSE] researchers reported that the best predictor of exacerbation was, by far, prior exacerbation. Other predictors were FEV1 decline, SGRQ-C, GERD and WBC.

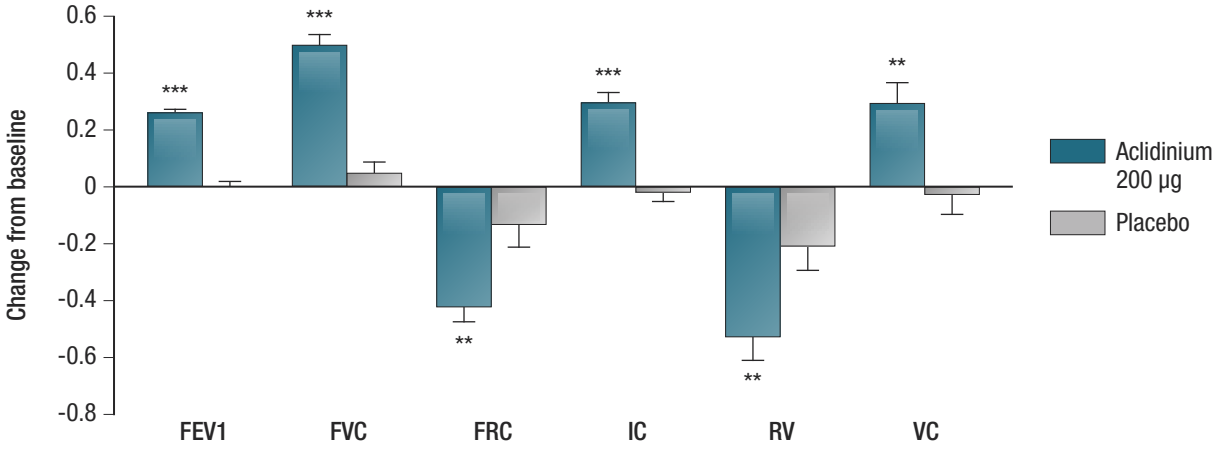
Another common topic of discussion at ERS 2010 was the increased risk of cardiovascular (CV) disease among patients with COPD, and the impact this has on the course of COPD.

One presenter discussed how spirometric data have been collected in the well known Framingham Heart Study since the 1940s.[17] This has allowed researchers to examine lung function in the context of CV disease and other CV risk factors. Some of the findings that have been presented over the years include the fact that the rate of FEV1 decline among smokers can be normalized if the individual quits smoking before the age of 30 years. If the individual quits after age 40, the decline is attenuated, but remains worse than for those who never smoked.

Framingham researchers have also found that higher blood-sugar levels are correlated with decreased lung function. Another COPD-related finding from the Framingham database is that CRP is the only biomarker correlated with COPD in multivariate analysis. Future directions for research with the Framingham data include a search for genotype-phenotype correlations. The Framingham genetic database is very large, now spanning three generations. To date, researchers have already identified several single nucleotide polymorphisms (SNPs) associated with lung function; the presence of each SNP is correlated to an approximate 50-75 mL reduction.

The impact of CV disease in COPD was also investigated by a Canadian group who presented their findings at ERS 2010.[18] These researchers sought to determine whether CV risk factors and underlying CV disease negatively impact length of hospital stay and readmission rate for exacerbations of COPD. They found that, of the 128 patients hospitalized for COPD exacerbations (283 admissions), CV comorbidities were common. In total, 44% had CV risk factors, 49% were taking CV medications, 30% had ECG abnormalities and 43% had diagnosed CV disease. The study showed that CV comorbidities contribute to prolonged hospital stay, causing the researchers to conclude that such comorbidities need to be actively addressed and managed during hospital admission for AECOPD.

FIGURE 4. **Aclidinium Bromide and Lung Function (2-hour Post-dose) in COPD**[22]



FEV1 = forced expiratory volume in one second; FVC = forced vital capacity; FRC = functional residual capacity; IC = inspiratory capacity; RV = residual volume; VC = ventilatory capacity.

THEME 4: New Research in COPD Management

The ERS 2010 meeting saw a wealth of new research in COPD management presented. This included research with well known, existing therapies and with novel, emerging therapies.

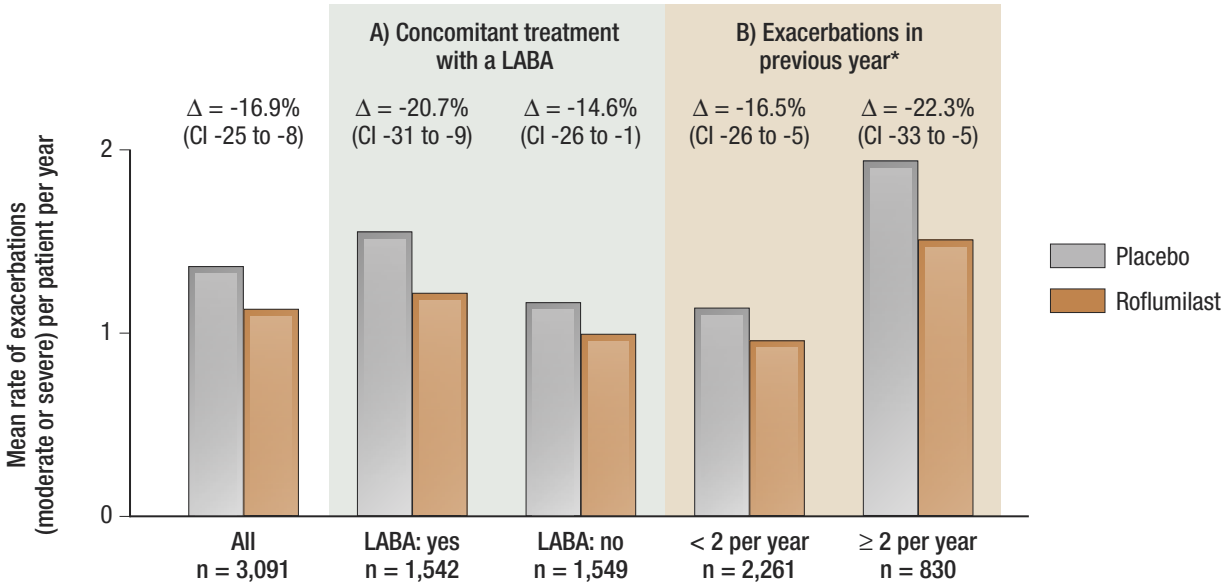
Established medications. Among the research presented which focused on existing medications were data from a group of American investigators who examined outcomes for COPD patients who had a COPD-related emergency-department visit (ED) or hospitalization. The investigators compared outcomes among patients who subsequently received combination inhaled corticosteroid and long-acting beta-agonist (ICS + LABA) treatment vs. those who received any other medical therapy.[19]

They reported that, after adjusting for baseline differences, the ICS + LABA combination (fluticasone + salmeterol) was associated with 21% significantly lower risk of any COPD exacerbation ($p < 0.05$) and 35% significantly lower risk of ED visit or hospital admission ($p < 0.05$). The time to any COPD event was significantly longer for the group receiving ICS + LABA combination. Furthermore, the adjusted median COPD-related monthly costs were significantly lower for the ICS + LABA group.

Another interesting finding with respect to ICS + LABA combination therapy for COPD was presented by a German-led group at ERS 2010.[20] Welte et al used a new questionnaire, the Capacity of Daily Living during the Morning (CDLM), to assess the effects of treatment on ability to perform morning activities of daily living. They presented findings from two studies using this instrument. They found that the formoterol + budesonide combination was associated with a clinically significant improvement on the CDLM (Figure 3). Another ICS + LABA combination, fluticasone + salmeterol, was also associated with improvement on the CDLM, but this improvement did not reach clinical significance.

> The study showed that CV comorbidities contribute to prolonged hospital stay, causing the researchers to conclude that such comorbidities need to be actively addressed and managed during hospital admission for AECOPD.

FIGURE 5. **Effect of Treatment with Roflumilast 500 µg or Placebo on Rate of Moderate or Severe Exacerbations in COPD[23]**



*COPD exacerbations in the previous years (based on patient recall).

Another study presented at ERS 2010 compared therapy with salmeterol vs. tiotropium in 7,376 patients aged > 40 years with more than 10 pack-years smoking history, an FEV1 < 70% predicted and more than one exacerbation in the previous year.[21] The investigators reported that, compared to salmeterol, tiotropium therapy was associated with a longer time to first exacerbation (hazard ratio [HR] 0.83, $p = 0.0001$); lower risk of premature cessation of therapy (HR 0.88, $p = 0.024$); and a lower risk of hospitalization for exacerbation (HR 0.72, $p < 0.0001$).

> The rate of exacerbations for patients treated with roflumilast was significantly lower than placebo regardless of which baseline therapy it was added to.

Novel agents. Evidence with many new and emerging agents was also presented at ERS 2010. The two of these agents with the best-developed clinical trial portfolio were roflumilast (an oral, highly selective phosphodiesterase 4 [PDE-4] inhibitor) and aclidinium bromide (a long-acting muscarinic antagonist).

An encouraging trial for aclidinium investigated its effects on resting lung function.[22] The study was designed to assess the effects of a 200-µg, once-daily dose on resting lung function at the end of the dosing interval, as well as on dyspnea and quality of life. The study enrolled 181 patients, who were treated with aclidinium or placebo for six weeks. As shown in Figure 4, active treatment resulted in significant improvements in several indicators of lung function. Aclidinium also significantly improved dyspnea scores, but no treatment differences were observed in terms of use of rescue medication.

The data presented with roflumilast are also compelling. One poster showed pooled efficacy data from two replicate, randomized, placebo-controlled, double-blind, multicentre trials in COPD patients with severe-to-very severe airflow obstruction, a history of exacerbations and chronic bronchitis.[23] As shown in Figures 5 and 6, the rate of exacerbations for patients treated with roflumilast was significantly lower than

placebo overall regardless of which baseline therapy it was added to.

The safety profile of roflumilast was also presented at ERS 2010, in terms of the results of a pooled analysis of 14 clinical studies involving 12,054 patients (more than 6,000 of whom received roflumilast).[24] The overall incidence of adverse events (AEs) (62.8% and 67.2%) and serious AEs (14.2% and 13.5%) were reported to be similar with placebo and roflumilast, respectively. The investigators did, however, note a difference in terms of weight changes, with roflumilast being associated with a -2.14 kg difference ($p < 0.0001$). This weight loss was most pronounced during the early (< 4 weeks) portions of the studies. Approximately two thirds of the weight loss was attributed to fat mass, and there was no significantly increased risk for weight loss among patients with low body mass index (BMI) at baseline.

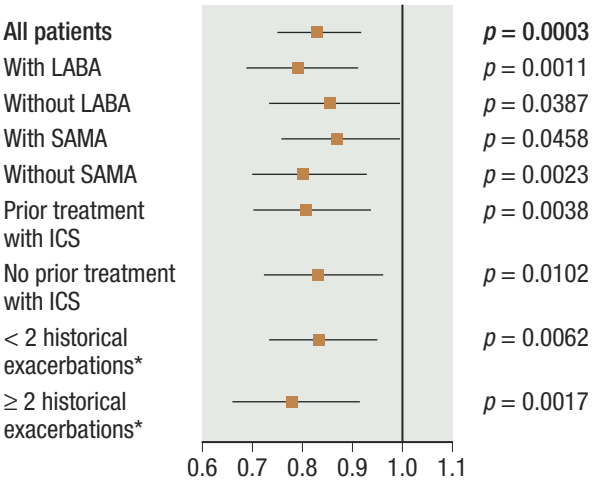
Another interesting finding with roflumilast presented at ERS 2010 was that this agent is associated with a significant decrease in glucose levels compared to placebo among patients with type 2 diabetes.[25]

The encouraging findings to date with roflumilast were also discussed in another symposium, entitled "A Deeper Look into COPD." Dr. Peter Barnes, one of this session's presenters, pointed out that roflumilast, which works by reducing systemic inflammation, operates through a mechanism of action that is distinct from other COPD therapies.[26] This systemic effect, he said, makes roflumilast the first lung-specific anti-inflammatory medication.

Older therapy, new findings. Two studies presented at ERS 2010 investigated the possible disease-modifying potential of the macrolide antibiotic, azithromycin, in COPD.[27,28] A randomized, double-blind, placebo-controlled study conducted by a Danish group involved the administration of azithromycin 500 mg once daily for three days every month over 36 months to 575 patients with moderate to severe COPD.[27] While the investigators did not observe any differences in terms of pulmonary function, azithromycin-treated patients had significantly fewer exacerbation days (at home or hospitalized) and significantly lower use of antibiotics and systemic steroids. These did not, however, translate into significant differences in terms of quality of life.

Another azithromycin study, by a Spanish group, was designed to determine whether chronic treatment with azithromycin (500 mg tid for 12 months) reduces the incidence of exacerbations, hospital admissions and days of hospital stay in patients with severe COPD.[28] In this much smaller study (n = 24), the investigators found that long-term daily azithromycin therapy significantly reduced the number of respiratory exacerbations, hospital admissions and days of hospital stay.

FIGURE 6. **Effect of Treatment with Roflumilast 500 µg on Reduction of Moderate or Severe COPD Exacerbations, by Subgroup**



*COPD exacerbations in the previous years (based on patient recall).

Rate ratios, 95% CIs and *p* values based on Poisson regression model with the following factors and covariates: treatment, age, sex, smoking status, baseline post-bronchodilator FEV1 (% predicted), study and country pool (only for the overall population). For all groups apart from LABA usage, concomitant treatment with LABAs was also included as a factor.

THEME 5: COPD Monitoring

Several studies presented at ERS 2010 attempted to elucidate novel ways to monitor COPD and response to therapy. Among these was a Canadian study evaluating the utility of a new tool—the three-minute, constant-pace shuttle walking test—to assess exertional dyspnea.[29]

The study was a randomized, controlled trial with a two-period crossover design. It involved 18 patients with GOLD stage II-III COPD, who were pre-treated with ipratropium bromide 500 µg or placebo and assessed with the three-minute test. The investigators reported that, in comparison to placebo, there was a statistically significant reduction in Borg dyspnea score with ipratropium during the walking test at 2 minutes, 2.5 minutes

and 3 minutes. They therefore concluded that this test was responsive to detect reductions in dyspnea following acute bronchodilation in COPD patients.

Conclusions

The annual meeting of the ERS—along with other major meetings like it—continues to be an important source of information for healthcare professionals interested in the management of patients with respiratory diseases. The 2010 ERS Congress offered a wealth of clinical-trial information and expert discussion on the diagnosis, classification, treatment and monitoring of COPD. For more information on the data presented in this summary, or for more information about other research presented at ERS 2010, visit the Congress website at *www.erscongress2010.org*.

References:

1. Kaplan A, Marciniuk D, Bouchard J, et al. Comfort in diagnosing COPD: A survey of Canadian physicians. Presented at the European Respiratory Society Annual Congress 2010. Poster P4241.
2. Postma DS. Genetics of Asthma and COPD. Presented at the European Respiratory Society Annual Congress 2010 as part of the symposium "Similarities and differences of asthma and COPD," September 20, 2010. Presentation 3333.
3. Saetta M. Immunologic aspects of asthma and COPD. Presented at the European Respiratory Society Annual Congress 2010 as part of the symposium "Similarities and differences of asthma and COPD," September 20, 2010. Presentation 3334.
4. Pavord I. Asthma and COPD: is the distinction important? Presented at the European Respiratory Society Annual Congress 2010 as part of the symposium "Similarities and differences of asthma and COPD", September 20, 2010. Presentation 3335.
5. Weiß G, Steinacher I, Lamprecht B, et al. Is the primary care (PC) office the right setting for spirometry to detect COPD? Presented at the European Respiratory Society Annual Congress 2010. Poster P4240.
6. Stocks J. Successes and failures of serial lung function assessments. Presented at the European Respiratory Society Annual Congress 2010 as part of the symposium "Unravelling the natural history of pulmonary function and COPD," September 19, 2010. Presentation 158.
7. Stanojevic S. Pooling lung function together: setting new standards. Presented at the European Respiratory Society Annual Congress 2010 as part of the symposium "Unravelling the natural history of pulmonary function and COPD," September 19, 2010. Presentation 160.
8. D'Urzo A, Tamari I, Bouchard J, et al. Variation among spirometry interpretation algorithms: Clinical implications. Presented at the European Respiratory Society Annual Congress 2010. Poster P4239.
9. Agusti A. Phenotypes of COPD: myths or reality? Presented at the European Respiratory Society Annual Congress 2010 as part of the symposium "Phenotypes and biomarkers: initial 3-year findings from the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) study," September 19, 2010. Presentation P1592.
10. Lomas D. Emerging biomarkers in COPD. Presented at the European Respiratory Society Annual Congress 2010 as part of the symposium "Phenotypes and biomarkers: initial 3-year findings from the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) study," September 19, 2010. Presentation P1593.
11. Barnes PJ. Independent view and Discussion. Presented at the European Respiratory Society Annual Congress 2010 as part of the symposium "Phenotypes and biomarkers: initial 3-year findings from the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) study," September 19, 2010. Presentation P1594.
12. Hurst JR, Vestbo J, Anzueto A, et al. Susceptibility to exacerbation in chronic obstructive pulmonary disease. N Engl J Med 2010; 363(12):1128-38.
13. Piquet J , Chavaillon J-M, Maurer C, et al. EABPCO-CPHG study: Prognosis factors of death and/or hospital admission in 1,142 patients, at 3 months after their admission to the pneumology department of a French general hospital for COPD acute exacerbation (AE). Presented at the European Respiratory Society Annual Congress 2010. Poster P539.
14. Lehouck A, Carremans C, Decramer M, et al. Muscle weakness and ADO-index determine length of hospital stay for an acute COPD exacerbation. Presented at the European Respiratory Society Annual Congress 2010. Poster P551.
15. Cano Aguirre M, Girón Moreno RM, Carbajo CM, et al. Mortality predictors in COPD exacerbation. Presented at the European Respiratory Society Annual Congress 2010. Poster P546.
16. Ekström M, Franklin K , Ström K, et al. Increased relative mortality in women with severe oxygen-dependent COPD. Presented at the European Respiratory Society Annual Congress 2010. Poster E1749.
17. O'Connor G: Framingham and other cardiovascular cohorts with lung function data. Presented at the European Respiratory Society Annual Congress 2010 as part of the symposium "Unravelling the natural history of pulmonary function and COPD," September 19, 2010. Presentation 159.
18. Lane C, Wong A, Burns J, et al. Acute exacerbations of chronic obstructive pulmonary disease: Impact of cardiovascular co-morbidities. Presented at the European Respiratory Society Annual Congress 2010. Poster E1745.
19. Mapel D, Shah M, D'Souza A, et al. Exacerbation rates and healthcare costs following hospitalizations and emergency department visits for COPD. Presented at the European Respiratory Society Annual Congress 2010. Poster E1746.
20. Welte T, Miravitlles M, Karlsson N, et al. Improving morning activities in COPD patients with budesonide/formoterol: Assessment of data from two randomised trials using minimal important differences from a morning activities questionnaire. Presented at the European Respiratory Society Annual Congress 2010. Poster P1202.
21. Vogelmeier C, et al. Reductions in COPD exacerbations with tiotropium compared to salmeterol. Presented at the European Respiratory Society Annual Congress 2010. Poster P5091.
22. Celli B, Maltais F, Casaburi R, et al. Aclidinium bromide improves resting lung function in patients with moderate to severe COPD. Presented at the European Respiratory Society Annual Congress 2010. Poster P1183.
23. Bateman E, Calverley PM, Fabbri LM, et al. Efficacy of roflumilast in patients with a history of frequent exacerbations: Pooled data from pivotal 12-month studies. Presented at the European Respiratory Society Annual Congress 2010. Poster P4003.
24. Calverley PM, Fabbri LM , Rabe KF, et al. Roflumilast in the treatment of COPD: A pooled safety analysis. Presented at the European Respiratory Society Annual Congress 2010. Poster P4001.
25. Wouters E , Teichmann P, Brose M, et al. Effect of roflumilast (ROF) on glucose levels in patients with COPD and diabetes mellitus type 2 (DM2). Presented at the European Respiratory Society Annual Congress 2010. Poster P4002.
26. Barnes PJ. Treatment of inflammation in COPD. Presented at the European Respiratory Society Annual Congress 2010 as part of the symposium "A Deeper Look into COPD," September 19, 2010. Presentation 1811.
27. Mygind LH, Pedersen C, Vestbo J, et al. A randomized, placebo-controlled 3 years study of prophylactic azithromycin in 575 patients with chronic obstructive pulmonary disease (COPD). Presented at the European Respiratory Society Annual Congress 2010. Poster P5580.
28. Casabon J, Pomares X, Monton C, et al. Long-term azithromycin therapy in severe COPD with repeated exacerbations. Presented at the European Respiratory Society Annual Congress 2010. Poster P542.
29. Sava F, Perrault H, Brouillard C, et al. Responsiveness of a 3-min shuttle walking exercise test to assess dyspnea in COPD. Presented at the European Respiratory Society Annual Congress 2010. Poster P1332.