ONLINE SUPPLEMENT

Assessment of the Primary Study Outcome

The study coordinators determined whether hospital admissions and/or ED visits for a COPD exacerbation occurred during the 6-month follow-up period using two strategies. First, coordinators regularly monitored the automated medical records of study subjects using the informatics system developed by BJC Healthcare (BJC Desktop, St. Louis, MO). BJC Healthcare is one of the largest nonprofit health care organizations in the United States, delivering services to residents primarily in the greater St. Louis, southern Illinois and mid-Missouri regions, and is made up of 13 hospitals and multiple community health locations. All inpatient, outpatient, and ED visits to a BJC affiliated institution are available real-time using BJC Desktop. Persons treated within this healthcare system are, in the majority of cases, readmitted to one of the system's participating hospitals. If a patient who receives healthcare in the system presents to a non-system hospital, he/she is often transferred back into the integrated system because of issues of insurance coverage. Second, the study coordinators conducted planned telephone inquiries to subjects in order to determine whether they had a recent hospitalization and/or ED visit and if so what the medical indication for that admission/ED visit was. When subjects had expired or were not available coordinators would speak with family members or surrogates to obtain this information.

Validation of the Study Outcome

An outcome adjudication committee made up of two investigators (MHK, RK) reviewed the study records of each subject with a hospital admission and/or ED visit to determine whether an exacerbation of the subject's underlying COPD was the reason for the hospital admission and/or ED visit, or if there was another cause.

Respiratory Therapist-Disease Management (RT-DM) Protocol

1) Verify that subjects' lung disease is COPD and not another type of pulmonary disorder. This required a review of inpatient and outpatient medical records. If pulmonary function studies

were not available the RT performed bedside spirometry in order to confirm the presence of COPD prior to randomization in all patients. If the diagnosis of COPD was questioned by the RT assigned to coordinate the subject's care, the diagnosis was reviewed by a board-certified pulmonary /critical care physician (MHK).

2) Review study subjects' medications to confirm that the prescribed therapy was consistent with the Department of Respiratory Care Services' guidelines for the management of COPD as well as being compliant with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines for disease management. Any discrepancies between subjects' ordered medical therapies and the above mentioned guidelines were discussed with the treating physicians to achieve compliance with these guidelines.

3) Determine the need for additional inpatient or outpatient therapies (e.g., pulmonary rehabilitation and/or exercise, noninvasive nocturnal ventilation) and/or diagnostic evaluations (e.g., exercise desaturation study, sleep study, comprehensive nutritional evaluation). Subjects assessed by the coordinating RT to require any of these additional therapies or evaluations had these recommendations documented in their inpatient medical records. Any unresolved treatment issues were settled by Dr. Kollef or the pulmonary inpatient consult service.

4) For all actively smoking subjects cessation counseling was provided. Additionally, the coordinating RT discussed the need for pharmacotherapy to aid with smoking cessation with the treating physicians (e.g., nicotine patch or gum).

5) A review of subjects' social situations was performed by the coordinating RTs to determine whether there were barriers present that impeded optimal outpatient management. These included inability to afford medications and lack of access to transportation services for outpatient appointments. When such factors were identified efforts were initiated to eliminate these barriers (e.g., referral to social work and case coordinators, prescription assistance,

providing pharmacy vouchers for bronchodilators and information on St. Louis City and St. Louis County transportation services for disadvantaged individuals).

RT-DM Action Plan

1) Insure that subjects received all of their medications and were properly instructed on the use of all medications including inhaled bronchodilators. This required hands-on training of the individuals before hospital discharge on technique for use of inhaled bronchodilators and subsequent sessions as deemed necessary by the RT.
2) Confirm that additional treatments and/or therapies were made available to the subject as determined by the physicians caring for them during their hospital stay. Such additional treatments and/or therapies included prescribed use of long-term oxygen therapy, non-invasive mechanical ventilation, outpatient physical therapy or rehabilitation therapy, access to smoking cessation programs, and carrying out any other diagnostic tests recommended and prescribed by the treating physicians (pulmonary function studies, sleep study, exercise desaturation study). The RT case manager assigned to the subject could also recommend specific adjunctive therapies, such as those noted above, to the treating physicians based on their assessment of the subject prior to hospital discharge.
3) Warrant that patients had timely follow-up visits arranged following hospital discharge. This required confirming that an outpatient follow-up visit had been arranged.
4) Confirm that subjects understood their action plan for self-treatment of exacerbations and that they understood when and where to seek medical attention due to an acute exacerbation of their COPD that was not responsive to the prescribed medical therapy outlined in their action plan. This included calling their primary care physician or the emergency department of Barnes-Jewish Hospital.
5) Conduct follow-up with the subjects with 5 planned telephone calls at 48-72 hours following discharge and at 7-10, 30, 90 and 180 days following discharge. For intervention subjects the phone calls were to determine whether the subject had any specific questions or

concerns related to their therapies, medical treatments or evaluations. During these calls the RTs also attempted to ascertain whether any ED visits or hospitalizations occurred at non-BJC Healthcare facilities and for what indications. Additional phone calls could be made by the RTs to intervention subjects at their discretion to facilitate access to medications and/or to insure access to follow-up medical visits. For control subjects the phone calls were only to ascertain whether any ED visits or hospitalizations occurred at non-BJC Healthcare facilities and for what indications.

6) Use the GOLD Guidelines to determine that appropriate controller medications were prescribed to subjects at the time of hospital discharge based upon disease severity as assessed by spirometry.

Multivariate Analysis

We confirmed the results of the univariate analysis demonstrating a relationship between hospital readmission for a COPD exacerbation and study group assignment, while controlling for specific subject characteristics (asthma, obstructive sleep apnea, use of leukotriene receptor antagonists, use of nasal corticosteroids, daily ethanol ingestion), using multiple logistic regression analysis. All variables entered into the model were assessed for co-linearity, and interaction terms were tested. The most parsimonious model was derived using the backward manual elimination method, and the best-fitting model was chosen based on the c-statistic. The model's calibration was assessed with the Hosmer-Lemeshow goodness-of-fit test. Results of logistic regression are presented as adjusted odds ratios with 95% confidence intervals. Linear regression was used to assess the relationship between the number of hospital readmissions for a COPD exacerbation and study group assignment while controlling for potential confounders.

Interim Analysis

An interim analysis was performed to evaluate safety of the protocol. The interim analysis was conducted by an independent data safety monitoring committee.