An updated model for prediction of asthma exacerbations using albuterol electronic multi-dose dry powder inhaler

Rajan Merchant,1 Guilherme Safiotti,2 Lena Granovsky,3 Michael Reich,2 Thomas Li,3 Taniah Hill,1 Randall Brown,4 Roy Pleasant,6 Giselle Mosaime,7 Michael DePietro1

1Woodland Clinic Medical Group, Allergy Department, Ogden, UT, USA; 2Teva Pharmaceutical Industries, Asaf-Hayehsharon Medical, Petah Tikva, Israel; 3Teva Pharmaceuticals, East Hanover, NJ, USA; 4Teva Branded Pharmaceutical Products R&D Inc., West Chester, PA, USA; 5Division of Pulmonary Medicine and Critical Care, University of North Carolina at Chapel Hill, School of Medicine, Chapel Hill, NC, USA; 6NorthShore University Health System, Evanston, IL, USA

Background

• Early detection of impending asthma exacerbations would provide opportunities for pre-emptive treatment and improve asthma action plans.1 Previous predictive models for asthma exacerbations have had a limited accuracy for imminent events.2

• A predictive model for impending exacerbations was successfully developed using data gathered from the ProAir® Digihaler™ (albuterol V9 gyygide, Figure 1), an electronic multi-dose dry powder inhaler (eMDPI) with integrated sensors.3

• Using additional patient information and baseline data, the initial model was refined to improve the predictive accuracy.

Methods

• The predictive model was developed using data from a 12-week, open-label study (NCT02969408), conducted between February 2017 and February 2018.

• Digihaler passively recorded time and date of albuterol use and inhalation parameters: peak inspiratory flow (PIF), time to inspirable volume, and inhalation duration.

• Data were downloaded from inhalers and analyzed at the end of the study (Figure 2).

• An exacerbation was defined as an event where the patient was required to increase their dose of oral corticosteroids and attended an unscheduled provider visit (e.g. urgent care visit, hospitalization).

• Machine learning modeling

• Case report form (CRF) data, such as medical history, body mass index (BMI), and blood pressure, were combined with Digihaler data and subjected to a machine learning algorithm to refine a model predictive of impending exacerbations.

Figure 1 ProAir Digihaler

• Algorithms were trained on patient-specific inhalation information collected from Digihaler such as age, BMI, blood pressure, and the number of exacerbations and hospitalizations in past 12 months

• Baseline features and features prior to prediction, comparison between the two, and trends of changes in these features were subjected to supervised machine learning algorithms.

• A 4-fold cross validation technique was used to compare performance metrics and gradient boosting trees were chosen as the best algorithm. The generated model was evaluated by receiver operating characteristic area under curve (ROC-AUC) analysis.

Results

• A total of 360 patients completed the study with >1 inhalation from Digihaler and were included in the analysis; of these, 64 patients experienced a total of 78 exacerbations.

• Demographics and inhalation characteristics for patients enrolled in the study are shown in Table 1

Table 1 Demographics and inhalation characteristics

Conclusions

• Digihaler data, including the inhalation characteristics, in combination with CRF information, resulted in an improvement of the 5-day exacerbation predictive model ROC AUC to 0.83.

• Additional studies, and potentially the inclusion of other data sources, will further refine the model and increase its predictive value.

• Real-life monitoring data collected via eMDPIs, such as the ProAir Digihaler, could help improve asthma management and enable pre-emptive interventions to minimize exacerbations, improve quality of care and reduce healthcare costs.