**Efficacy and Safety of Extrafine Particle Inhaled Corticosteroids in a Veteran Population**

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**Abstract**

**Background:** In recent years, the Durham Veterans Affairs Health Care System (DVAHCS) has seen an increase in prescriptions for extrafine particle inhaled corticosteroids (ICS) in the treatment of asthma, chronic obstructive pulmonary disease (COPD), and asthma-COPD overlap syndrome (ACOS). This study aims to determine the efficacy and safety of extrafine particle ICS in a real-world study of this patient population.

**Methods:** This was a retrospective pre-and post-intervention cohort study conducted within the DVAHCS. Veteranswith a diagnosis of chronic asthma, COPD, or ACOS who were prescribed an extrafine particle ICS were eligible for inclusion unless their pulmonary prescriptions were written by a non-VA provider, they were receiving chronic prednisone, they had a diagnosis of COVID-19, or they lacked spirometry measurements within 10 years prior to the prescription index date. Veterans prescribed an extrafine particle ICS between January 1, 2015 and June 30, 2021 were identified and stratified into one of two groups for all primary and secondary objectives: 1) those who initiated step-up therapy with an extrafine particle ICS (ie, extrafine particle added to fine particle or 2) those who switched from fine particle ICS to extrafine particle ICS. The primary objective of this study was to determine if a difference exacerbations for airway disease exists by determining the difference in pre- vs. post- exacerbation category (rank of 1 for 0 exacerbations, 2 for 1-2, and 3 for 3 or more). Safety endpoints evaluated the incidence of most common ICS adverse events as well as reasons for ICS inhaler discontinuations.

**Results:** 116 of 238 patients screened met criteria for inclusion. Most patients in the study were male and the average age was ~69 years. COPD was the most common airway disease diagnosis, followed by ACOS, then asthma. For the primary endpoint, there was a statistically and clinically meaningful decrease in the post-intervention timeframe compared to pre-intervention timeframe for patients in the step-up group at 6 months (57 vs. 40 patients had no exacerbations after initiation of the extrafine particle ICS; 16 vs. 26 had 1-2 exacerbations, and 2 vs. 9 had 3 or more exacerbations). There was also a significant difference at the 12 month timepoint. There was no significant difference for patients in the switch group at 6 or 12 months. For the safety endpoints, incidence of pneumonia and oral/esophageal candidiasis was relatively low in both the pre- and post-intervention timeframes, occurring with ~10% or less incidence. ICS inhaler discontinuations were most commonly due to patient or provider preference, as opposed to a true adverse drug reaction.

**Conclusions:**

Patients experiencing frequent airway disease exacerbations may benefit from addition of an extrafine particle ICS therapy. Stable patients may tolerate comparable-to-lower daily ICS doses with a switch to extrafine particle ICS therapy. ICS therapies were generally well tolerated. Future studies are needed to further elucidate which airway disease diagnoses are most likely to benefit. Ideal ICS dose requirements should be determined that both prevent exacerbations and avoid adverse reactions.