Efficacy and Safety of Omalizumab in Patients With Moderate-to-Severe Persistent Asthma Poorly Controlled on High-Dose Inhaled Corticosteroids and Long-Acting Beta-Agonists—Results of a Phase IIIb Randomized Controlled Trial

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Rationale: Omalizumab is an injectable monoclonal antibody that binds to IgE and is indicated for the treatment of patients 12 years and older with moderate to severe allergic asthma. In this study, patients with moderate-to-severe asthma poorly controlled on high-dose inhaled corticosteroids (ICS) and long-acting beta-agonists (LABAs) ± other controller medications, were treated with either omalizumab or placebo for 48 weeks.

Methods: 850 patients, 12-75 years old with poorly controlled moderate-to-severe asthma (defined as symptomatic with at least one asthma exacerbation in the preceding year despite taking high-dose ICS equivalent to ≥500 mcg fluticasone BID and a LABA) were enrolled. Omalizumab (n=427) or placebo (n=423) was added to existing medications for 48 weeks. The primary endpoint was the rate of protocol defined asthma exacerbations over the study period. Secondary efficacy endpoints included the change from baseline to Week 48 in mean daily number of puffs of albuterol, mean total asthma symptom score, and mean overall asthma quality of life as measured by overall standardized asthma quality of life score (AQLQs).

Results: The mean % predicted FEV1 (SD) at baseline was 64.9% (14.6) and patients had an average of 2 asthma exacerbations requiring systemic steroids, in the preceding year. Seven percent of patients had past history of intubation due to asthma exacerbations. Patients required a mean (SD) of 4.06 (3.02) puffs of albuterol per day, had mean total asthma symptom score of 3.89 (1.77) and an overall AQLQs of 3.92 (1.10). Approximately, 79% of patients completed the study. Patients receiving omalizumab had a significant reduction in the rate of asthma exacerbations at 48 weeks compared to patients receiving placebo (.66 vs .88, p=0.006). The change in mean number of puffs of albuterol per day (-1.58 vs -1.31, p=0.090) and mean total asthma score (-1.56 vs -1.30 and p=0.038) favored omalizumab vs placebo but did not achieve statistical significance at 48 weeks after adjusting for multiple comparisons. There was a statistically significant improvement in mean overall AQLQs score (1.15 vs 0.92, and p=0.005). Similar percentages of AEs (80.4% vs 79.5) and SAEs (9.3 vs 10.5%) were observed in the omalizumab versus placebo groups, respectively.

Conclusions: Our results demonstrate that long-term treatment with omalizumab is safe and can significantly reduce the rate of asthma exacerbations by 25% in patients with poorly controlled moderate-to-severe allergic asthma, despite receiving aggressive asthma controller therapy (high dose ICS + LABA).