EFFECT OF TEZEPELUMAB ON LUNG FUNCTION IN PATIENTS WITH SEVERE, UNCONTROLLED ASTHMA IN THE PHASE 3 NAVIGATOR STUDY

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Purpose: Tezepelumab is a human monoclonal antibody that blocks the activity of thymic stromal lymphopoietin (TSLP). In the phase 3 NAVIGATOR study (NCT03347279), tezepelumab significantly reduced exacerbations in patients with severe, uncontrolled asthma. We report the effects of tezepelumab on pre-bronchodilator (BD) forced expiratory volume in 1 second (FEV1) and other measures of lung function in NAVIGATOR.

Methods: NAVIGATOR was a multicenter, randomized, double-blind, placebo-controlled study. Patients (12–80 years old) receiving medium- or high-dose inhaled corticosteroids and ≥ 1 additional controller medication with or without oral corticosteroids were randomized 1:1 to receive tezepelumab 210 mg or placebo subcutaneously every 4 weeks for 52 weeks. The least-squares (LS) mean change from baseline was estimated at weeks 2 and 52 for the following endpoints using a repeated measures model: pre-BD FEV1, pre-BD forced vital capacity (FVC), pre-BD FEV1/FVC ratio and pre-BD forced expiratory flow at 25–75% of the FVC (FEF25–75).

Results: Overall, 1059 patients received treatment (tezepelumab 210 mg, n = 528; placebo, n = 531). At baseline, in the tezepelumab and placebo groups, respectively, the mean (standard deviation) pre-BD FEV1 was 1.83 L (0.72) and 1.85 L (0.71), pre-BD FEV1 % predicted normal was 62.8% (18.0) and 62.7% (18.0), pre-BD FVC was 2.89 L (0.93) and 2.95 L (0.91), pre-BD FEV1/FVC ratio was 63.16% (13.30) and 62.53% (12.91) and pre-BD FEF25–75 was 1.13 L/s (0.82) and 1.13 L/s (0.87). At week 2, the change from baseline was greater with tezepelumab vs placebo for pre-BD FEV1 (0.16 L vs 0.05 L; LS mean difference 0.11 L [95% confidence interval (CI): 0.07–0.15]), pre-BD FVC (0.16 L vs 0.06 L; LS mean difference 0.10 L [95% CI: 0.05–0.15]), pre-BD FEV1/FVC ratio (2.40% vs 0.51%; LS mean difference 1.89% [95% CI: 1.15–2.63]) and pre-BD FEF25–75 (0.16 L/s vs 0.05 L/s; LS mean difference 0.12 L/s [95% CI: 0.06–0.17]). At week 52, the change from baseline was greater with tezepelumab vs placebo for pre-BD FEV1 (0.23 L vs 0.10 L; LS mean difference 0.13 L [95% CI: 0.08–0.18]), pre-BD FVC (0.24 L vs 0.11 L; LS mean difference 0.13 L [95% CI: 0.07–0.19]), pre-BD FEV1/FVC ratio (2.59% vs 0.53%; LS mean difference 2.06% [95% CI: 1.22–2.90]) and pre-BD FEF25–75 (0.21 L/s vs 0.08 L/s; LS mean difference 0.13 L/s [95% CI: 0.07–0.19]).

Conclusions: Compared with placebo, treatment with tezepelumab resulted in rapid improvement of lung function in a broad population of patients with severe, uncontrolled asthma. Improvements in lung function parameters were observed by week 2 and sustained over 52 weeks.

Clinical Implications: This analysis reinforces existing evidence that tezepelumab rapidly improves lung function and sustains improvements over 52 weeks in patients with severe, uncontrolled asthma, further supporting its benefits in this patient population.

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