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Rademikibart in moderate-to-severe asthma: Impact of eosinophils and regional differences on response

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INTRODUCTION: In asthma trials the efficacy in Eastern European countries, notably Poland, has been reported as lower than in other regions (Jackson DJ et al. N Engl J Med. 2024;391:2337-2349). Rademikibart, an IL-4R α blocker, improves lung function rapidly, with effects sustained through 24 weeks (Kerwin E et al. Eur Respir J. 2024;64(suppl 68):OA2781). This post hoc analysis compared rademikibart efficacy in Polish versus non-Polish sites and by baseline blood eosinophil (EOS) count (<300 vs. $\geq$ 300 cells/ μ L).

METHODS: In this Phase 2 trial (NCT04773678), 322 participants with uncontrolled moderate-to-severe asthma were randomized 1:1:1 to rademikibart 150 mg Q2W (n=106), 300 mg Q2W (n=108), or placebo (n=108). The primary endpoint was absolute change in pre-bronchodilator (pre-BD) FEV₁ at Week 12. This analysis focuses on the expected Phase 3 dose, 300 mg Q2W.

RESULTS: In the full study population, rademikibart 300 mg improved pre-BD FEV₁ versus placebo (189 mL placebo-adjusted [PA], p<0.001), with greater benefit in participants with EOS $\geq$ 300 (328 mL PA, p<0.001). Non-Polish sites showed similar significant improvements (245 mL PA, p<0.0001; EOS $\geq$ 300: 391 mL PA, p<0.0001). However, in Poland, placebo responses exceeded treatment (-87 mL PA, p=0.497; EOS $\geq$ 300: -116 mL PA, p=0.664).

CONCLUSION: Overall, rademikibart rapidly and significantly improved lung function, with greater benefits in patients with higher eosinophils. Participants from Poland demonstrated greater placebo responses across all eosinophil strata. The unexpected Polish placebo response indicates regional differences affecting treatment outcomes and suggests a stronger response with rademikibart than first reported.