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Improved Lung Function and Asthma Control Observed with Rademikibart in Patients with Moderate-to-Severe Uncontrolled Asthma (CBP-201-WW002)

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Rationale: More than 26 million Americans are burdened with asthma symptoms. Rademikibart (formally, CBP-201), an IL-4R α -blocker, blocks both interleukin-4 and interleukin-13 signaling. We assessed rademikibart's efficacy and safety in patients with uncontrolled moderate-to-severe asthma.

Methods: This Phase 2b trial (NCT04773678) was a global, placebo-controlled study conducted in 79 sites with 322 patients randomized 1:1:1 to rademikibart 150 mg every two weeks (Q2W; n=106), 300 mg Q2W (n=108) each with a loading dose of 600 mg or placebo (n=108). Two-thirds of patients were treated in the United States. The primary end point was absolute change in the forced expiratory volume in 1 second (FEV₁) at Week 12 before bronchodilator (Pre-BD) use in the overall trial population. Additional end points included FEV₁ in patients with a blood eosinophil count of ≥ 300 cells/ μ L, mean percent predicted FEV₁ values at Week 12, and the exacerbation rates. Asthma control and safety were also assessed.

Results: Pre-BD FEV₁ at Week 12 was improved with both rademikibart doses. Further improvement was achieved in patients with eosinophil levels of ≥ 300 cells/ μ L (see table). Significant improvements started in Week 1 (p<0.001, both doses) and were sustained through 24-weeks of treatment (p=0.001 and p<0.001, respectively). Mean percent predicted FEV₁ improvement was observed at Week 12 with a 7.9% improvement over placebo with the 150 mg dose and 9.1% improvement with the higher dose. Placebo-adjusted changes from baseline in the Asthma Control Questionnaire (ACQ) score at Week 24 were -0.44 (p<0.001) and -0.33 (p<0.01), respectively. Improvement was evident as early as Week 1 and statistically significant starting at Week 2 through Week 24 for both doses. Although not powered to detect differences in exacerbations, strong trends toward prolonging the time to first exacerbation and overall reduced exacerbations were observed. More than half of all exacerbations during the 24-week study occurred in the placebo group (26 vs. 11 and 13 in patients receiving rademikibart, respectively). Treatment with rademikibart was generally well tolerated. Treatment emergent adverse events (TEAEs) were relatively similar across all groups, with the most common TEAEs being COVID-19, cough, dyspnea, and wheezing.

Conclusions: The trial met the primary endpoint of improvement in lung function with both rademikibart doses which were observed rapidly within the first week of treatment. Strong and significant improvement in asthma control was also observed. Rademikibart could benefit a substantial group of uncontrolled asthmatic patients who struggle for asthma control and freedom from exacerbations.

	Full Analysis Set (primary endpoint)			Patients with baseline Eosinophils ≥ 300 cells/μL (exploratory endpoint)		
		Rademikibart Q2W			Rademikibart Q2W	
	Placebo (n=96)	150 mg (n=96)	300 mg (n=86)	Placebo (n=37)	150 mg (n=33)	300 mg (n=41)

LS Mean Change from Baseline in pre-BD FEV ₁ at Week 12	95 mL	235 mL	284 mL	-8 mL	235 mL	320 mL
Difference in LS Means		140 mL (p = 0.005)	189 mL (p < 0.001)		243 mL (p < 0.001)	328 mL (p < 0.001)