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Title of Presentation	Improvement of Symptom Burden in Summit: Bezuclastinib in Adults with Non-Advanced Systemic Mastocytosis
abstract-hint	
Abstract of Presentation	Background: Patients with non-advanced systemic mastocytosis (NonAdvSM) often experience severe, debilitating symptoms that can significantly impair their quality of life. KIT c.2447 C>T (p.D816V) mutations are found in most patients with SM. Bezuclastinib, an oral, potent type 1 tyrosine kinase inhibitor with selective activity against KIT p.D816V, is being investigated in the Summit trial. Here, we report the effect of bezuclastinib on individual symptoms and symptom domains in Summit. Methods: Summit (NCT05186753) is a multicenter, randomized, double-blind, placebo-controlled phase 2 trial in patients with NonAdvSM who have inadequate symptom control despite best supportive care. Patients reported on their symptom severity (scored from 0 to 10 [most severe]) daily using the Mastocytosis Symptom Severity Daily Diary (MS2D2). The MS2D2 consists of 11 symptoms grouped into 4 domains (skin, fatigue, neurocognitive, and GI/pain). Results: Among 119 patients randomized to bezuclastinib and 60 randomized to placebo, mean domain severity at baseline (scored 0 to 10 [most severe]) was 7.3 (bezuclastinib arm)/6.8 (placebo arm) in the fatigue domain, 5.6/5.0 in the neurocognition domain, 5.4/5.2 in the skin domain,

	and 4.3/3.8 in the gastrointestinal/pain domain. Improvement with 24 weeks of bezuclastinib was seen in all domains. Patients' most severe symptoms had a mean severity of 8.1 in the bezuclastinib arm and 7.9 in the placebo arm, and significantly improved by 24 weeks of treatment with bezuclastinib. Conclusions: In the Summit study, patients with NonAdvSM treated with bezuclastinib reported consistent improvements across all domains and symptoms, including the most severe.