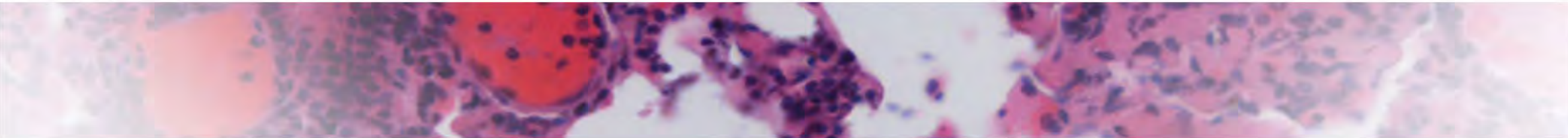




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The Effect of Bezucclastinib on the Pathobiology of Mastocytosis: Changes in BM Mast cells, Tryptase, and KIT p.D816V Variant Allele Frequency From the Pivotal Summit Trial

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Bezuclastinib, A Selective TKI, Has Demonstrated Efficacy and Tolerability in Patients with NonAdvSM in the Summit Clinical Study

- NonAdvSM is primarily driven by KIT p.D816V mutation and is defined by pathologic features
- Bezuclastinib is a selective type 1 tyrosine kinase inhibitor that is highly active against KIT p.D816V, has minimal brain penetration and spares closely related kinases
- Summit, a phase 2, randomized, placebo-controlled study evaluating bezuclastinib in NonAdvSM, demonstrated efficacy, safety, and tolerability¹
 - Bezuclastinib provided significantly greater symptom improvement vs placebo (Week 24 MS2D2 TSS LS mean change: -24.3 vs -15.4, $p < 0.001$)
 - Bezuclastinib demonstrated a favorable and manageable safety profile

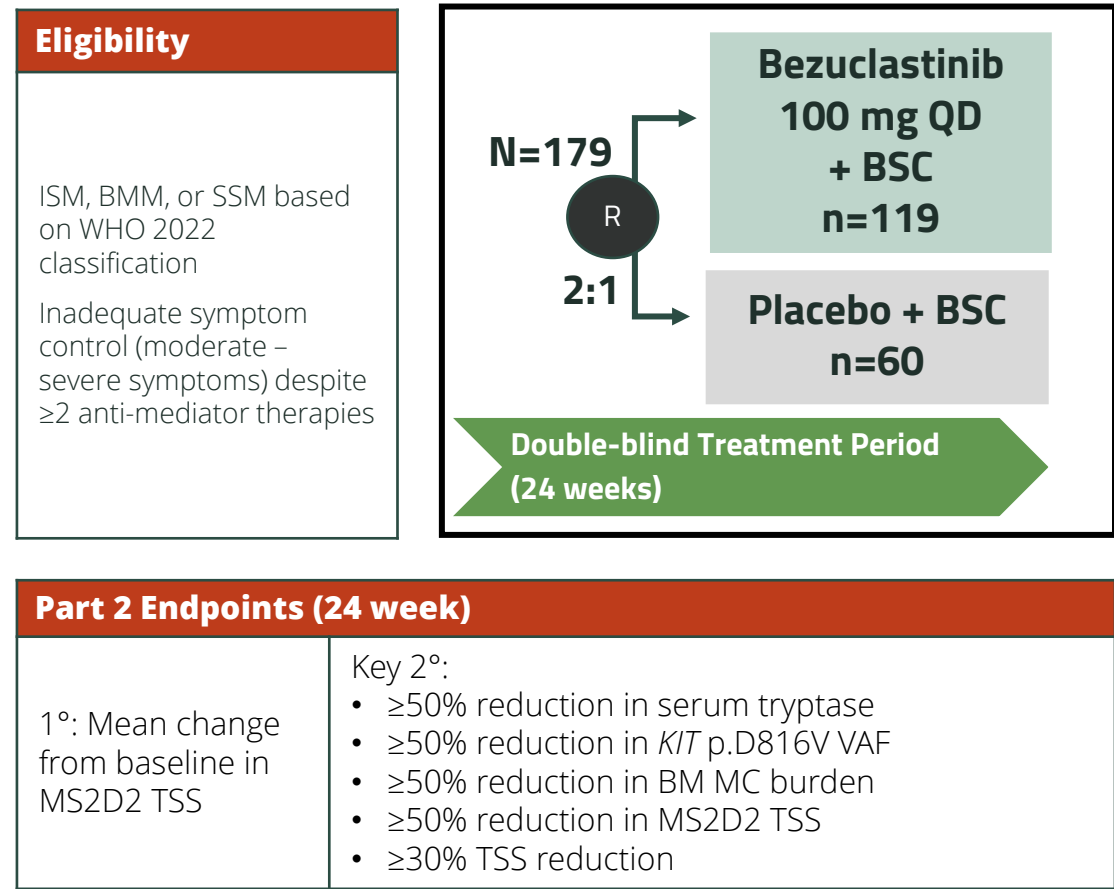
The goal of this analysis is to further assess the impact of bezuclastinib on the underlying disease pathology in Summit Part 2

LS mean, least squares mean; MS2D2, mastocytosis symptom severity daily diary; NonAdvSm, nonadvanced SM; SM, systemic mastocytosis; TKI, tyrosine kinase inhibitor; TSS, total symptom score.

1. Rein L et al. Presented at: ASH Annual Meeting 2025. Orlando, FL, 2025.

Study Design and Baseline Disease from Summit (NCT05186753), A Pivotal Phase 2 Study Evaluating Bezuclastinib in NonAdvSM

SUMMIT PART 2



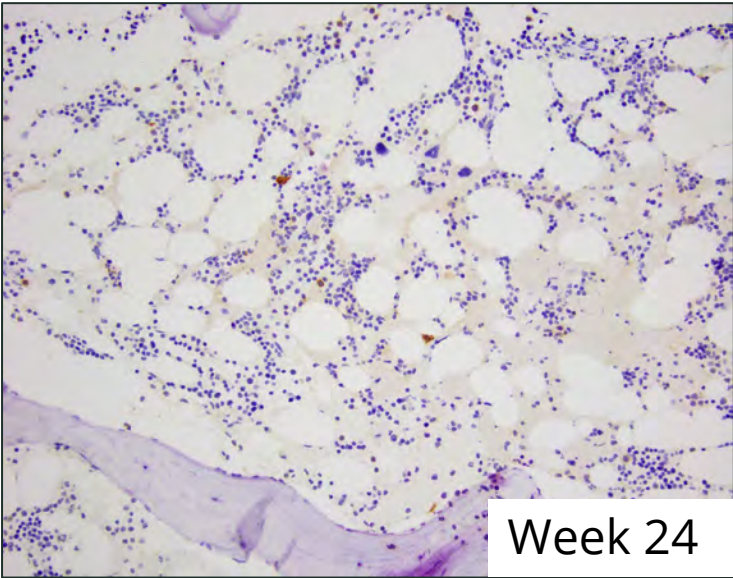
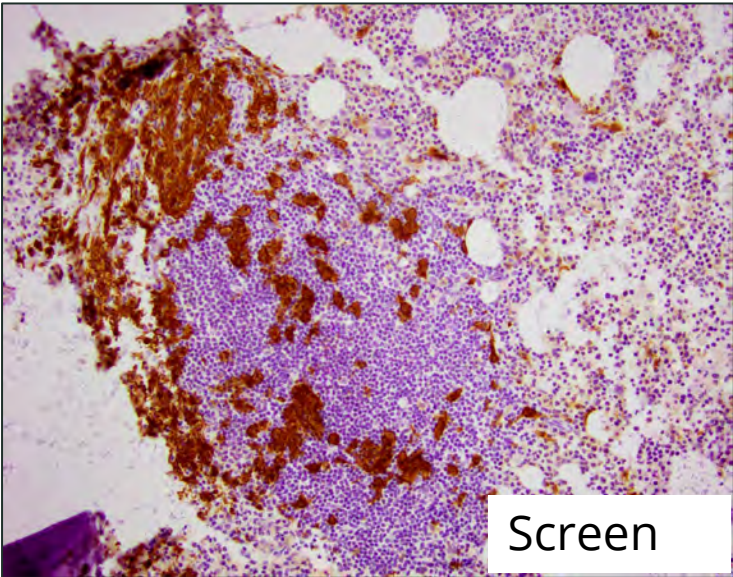
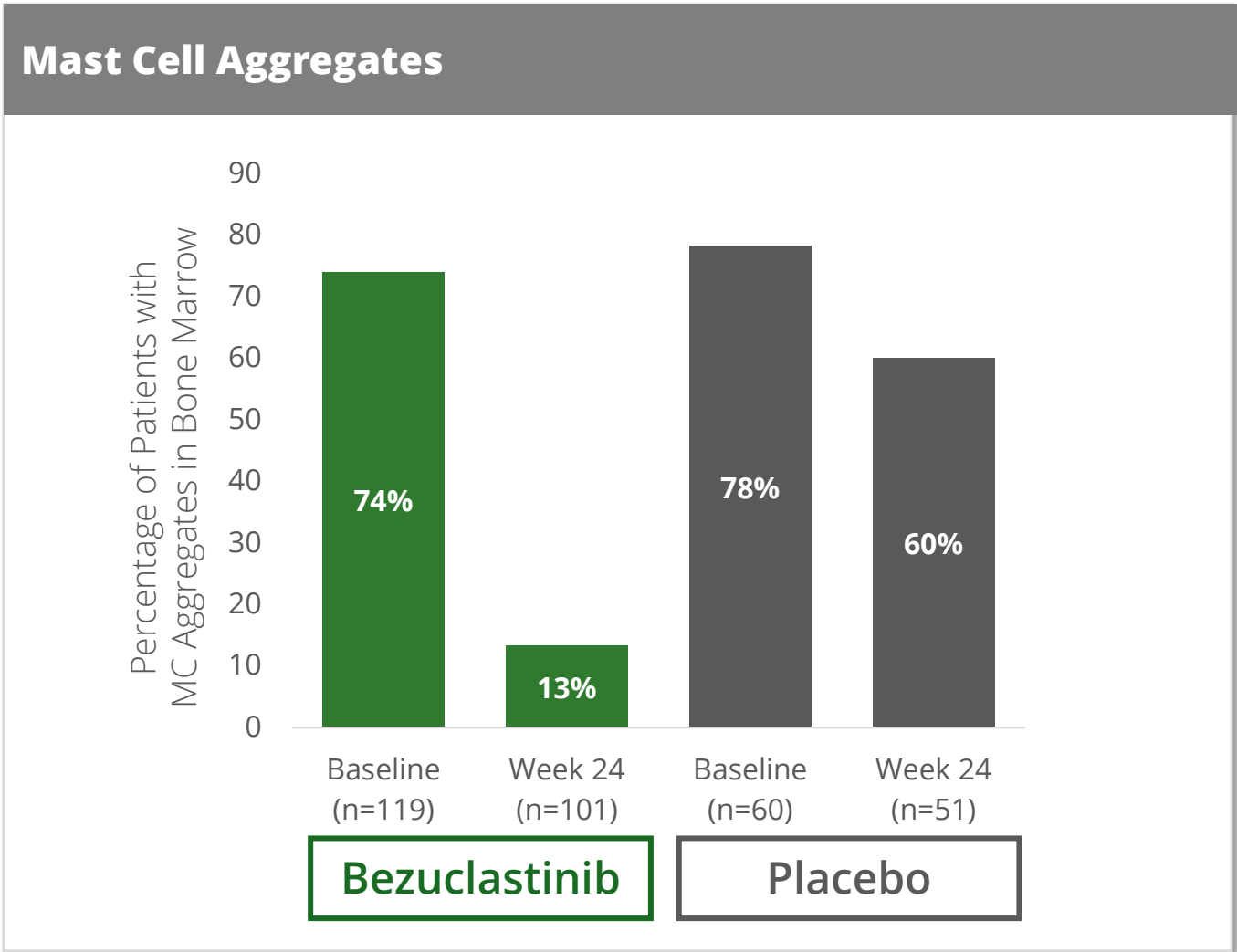
SUMMIT BASELINE CHARACTERISTICS

Demographics, Clinical Characteristics, and Disease Burden

	Bezuclastinib 100 mg QD (N=119)	Placebo (N=60)
Female, n (%)	74 (62.2)	44 (73.3)
Median Age in years, (range)	51 (24 – 73)	52 (23 – 78)
NonAdv Subtype, n (%)		
ISM	97 (81.5)	50 (83.3)
SSM	8 (6.7)	4 (6.7)
BMM	14 (11.8)	6 (10.0)
<i>KIT</i> p.D816V ^a in Whole Blood, Detected, n (%)	91 (76.5)	48 (80.0)
Median <i>KIT</i> p.D816V VAF ^a , % (range)	0.22 (0 ^b – 32.28)	0.30 (0 ^b – 33.59)
Median BM MC Burden, % (range)	10 (1 – 75)	10 (1 – 75)
Median Serum Tryptase, ng/mL (range)	39 (6.3 – 448)	41.2 (7.1 – 692)
Myelofibrosis grade, n (%)		
MF-0	45 (37.8)	22 (36.7)
MF-1	33 (55.0)	33 (55.0)
MF-2	10 (8.4)	3 (5.0)
MF-3	0	1 (1.7)

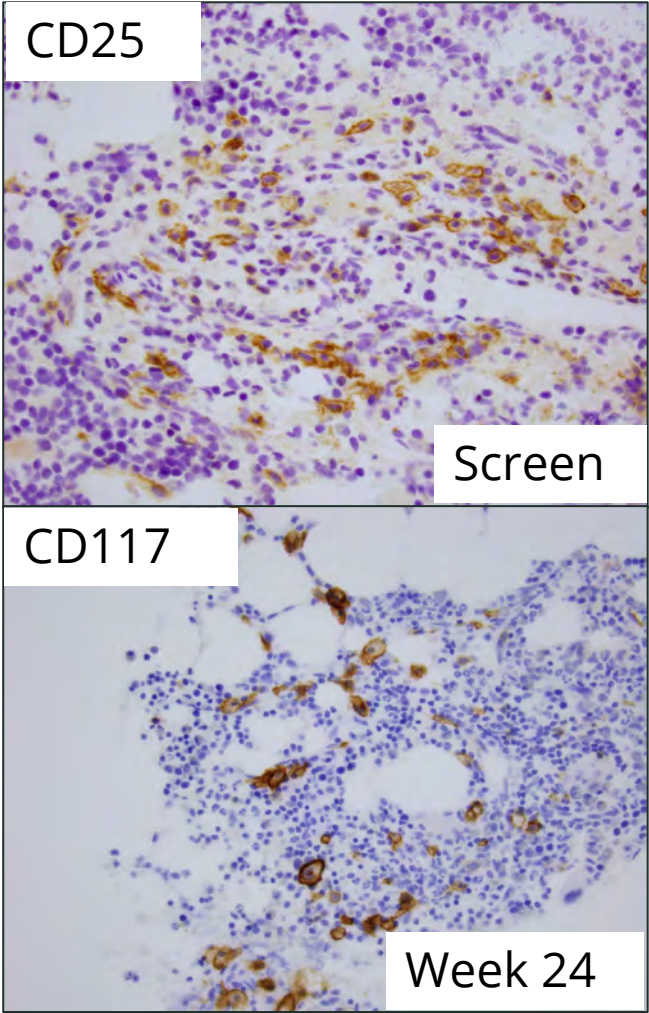
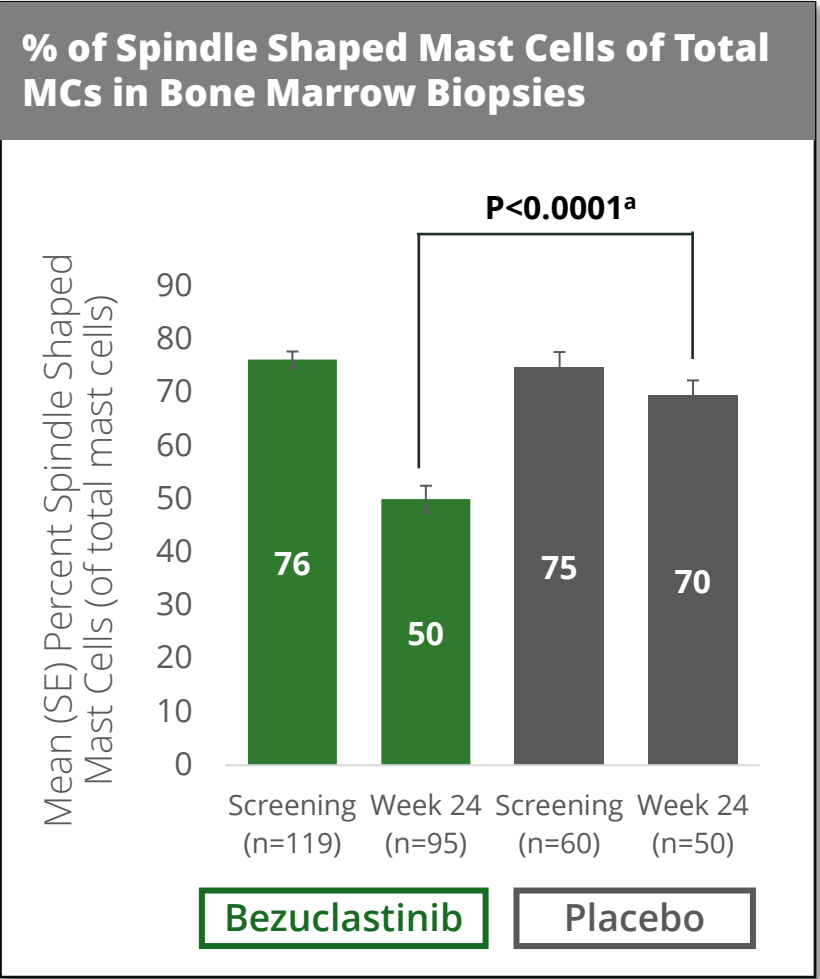
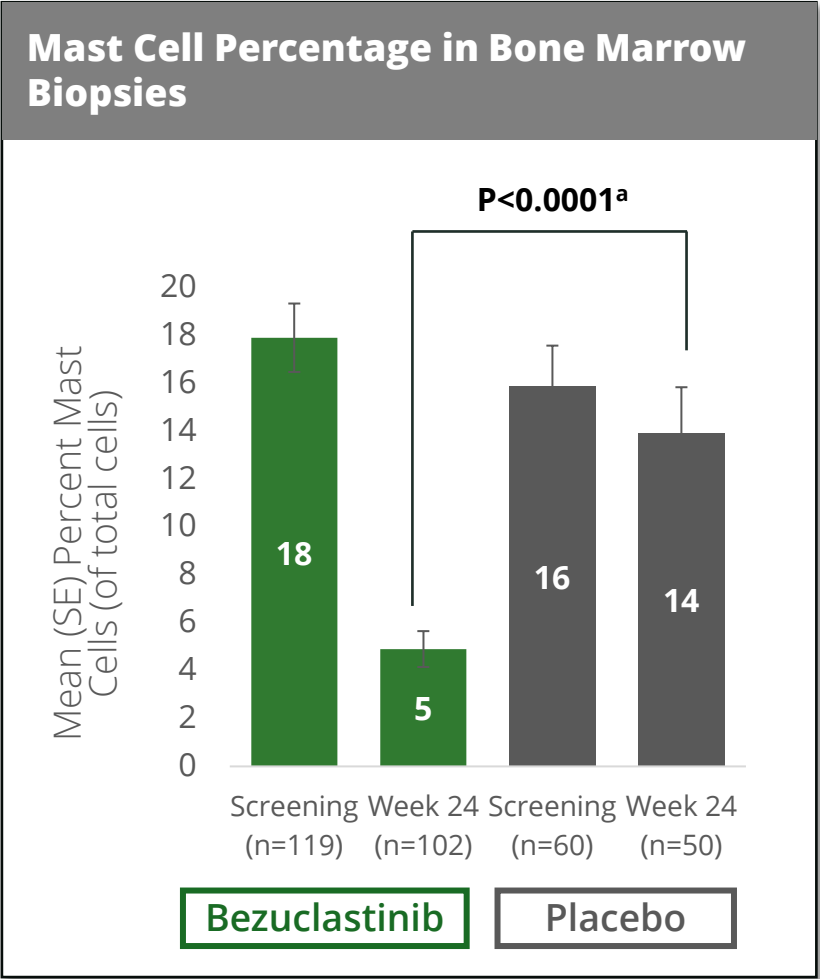
^alimit of detection equals 0.03%; ^bundetected.
BM, bone marrow; BMM, bone marrow mastocytosis; BSC, best standard care; ISM, indolent SM; MC, mast cell; MS2D2, mastocytosis symptom severity daily diary; QD, daily; SSM, smoldering SM; TSS, total symptom score; WHO, World Health organization.

Bezuclastinib Treatment Resulted in Clearance of Pathologic Mast Cell Aggregates, the Major Criterion for SM Diagnosis, From the Bone Marrow



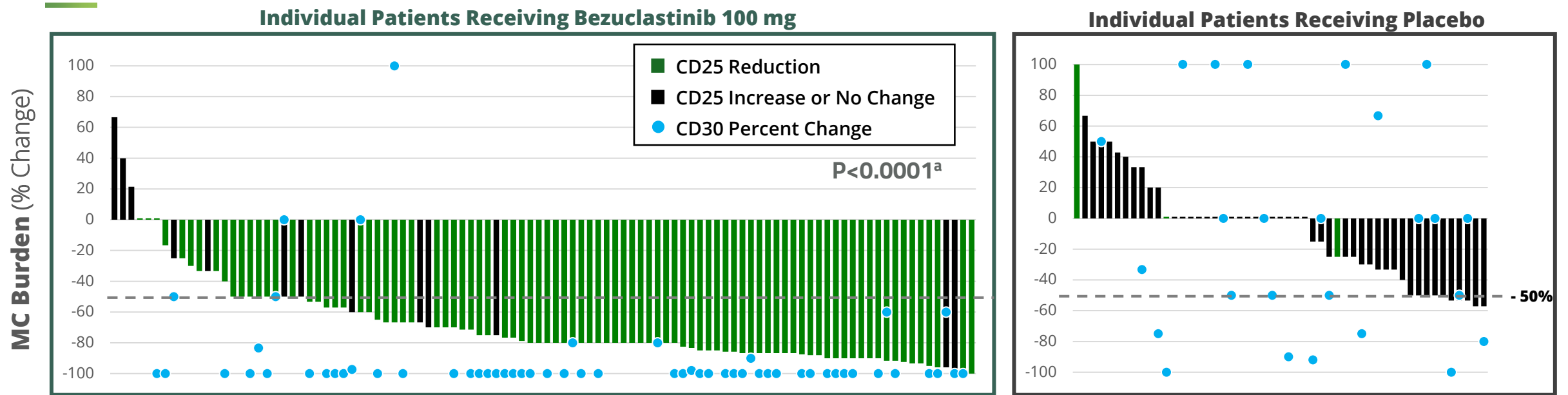
CD117

Bezuclastinib Treatment Resulted in Reduction and Normalization of Mast Cells Present in the Bone Marrow



^a P-value is calculated with a two sample t-test of change from baseline in bezuclastinib vs. placebo
Data cutoff: May 22, 2025

Bezuclastinib Reduced Bone Marrow Mast Cell Burden and Aberrant Expression of CD25 and CD30

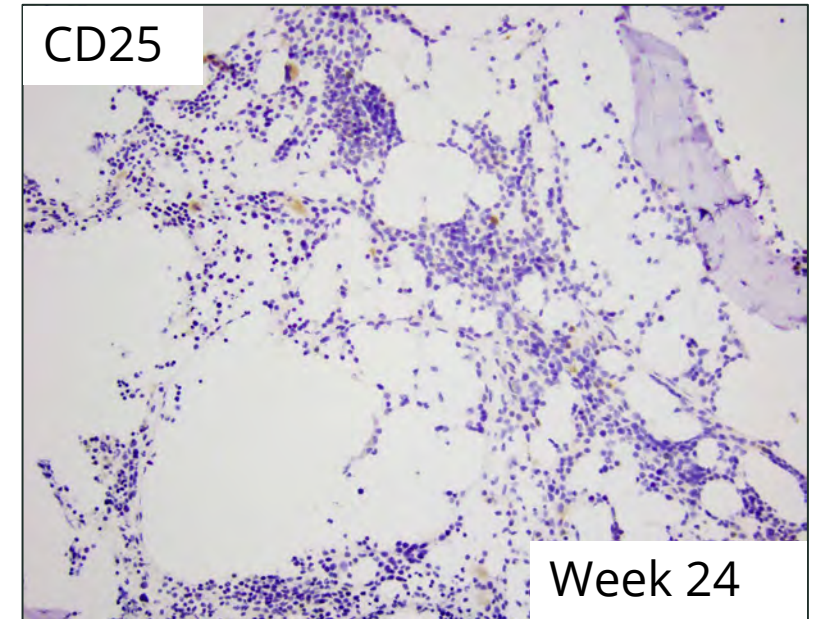
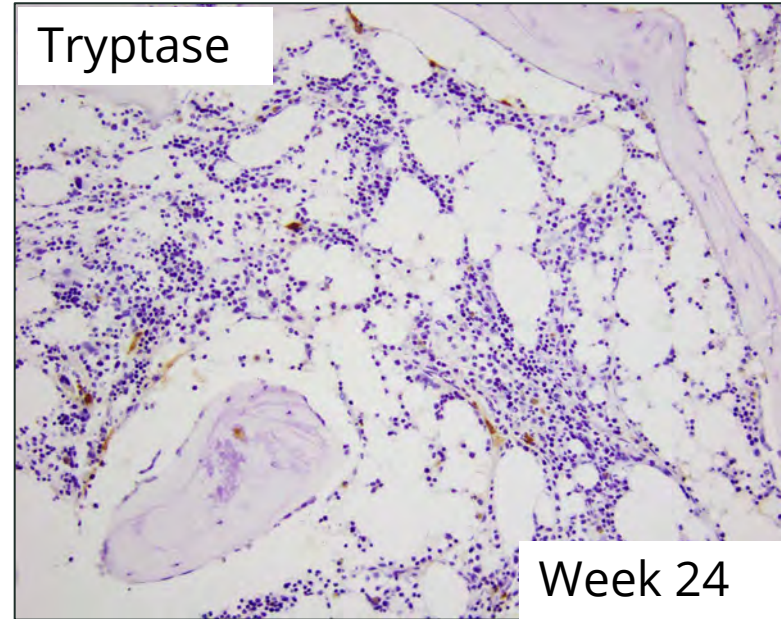
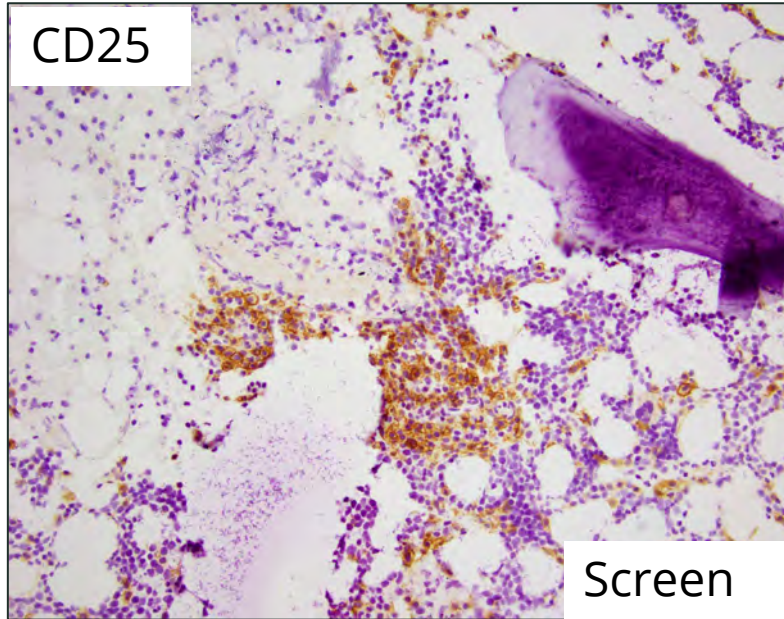


- Reduction in CD25 and CD30 expression supports targeted mast cell modulation and disease impact in NonAdvSM

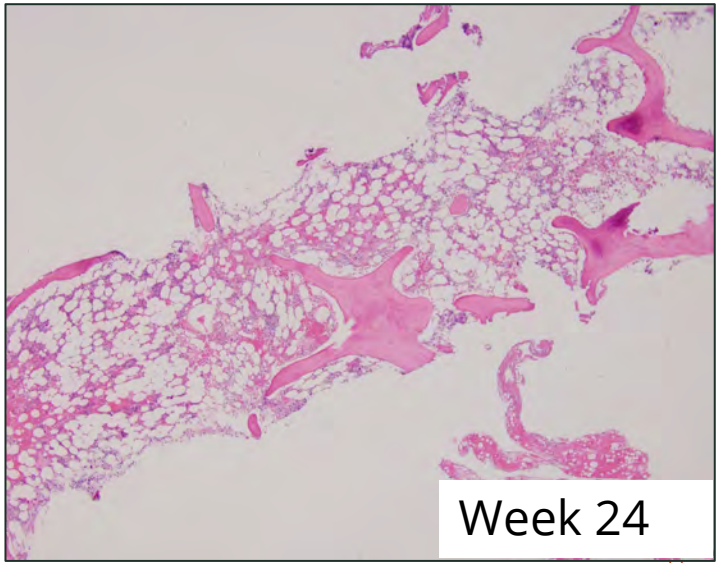
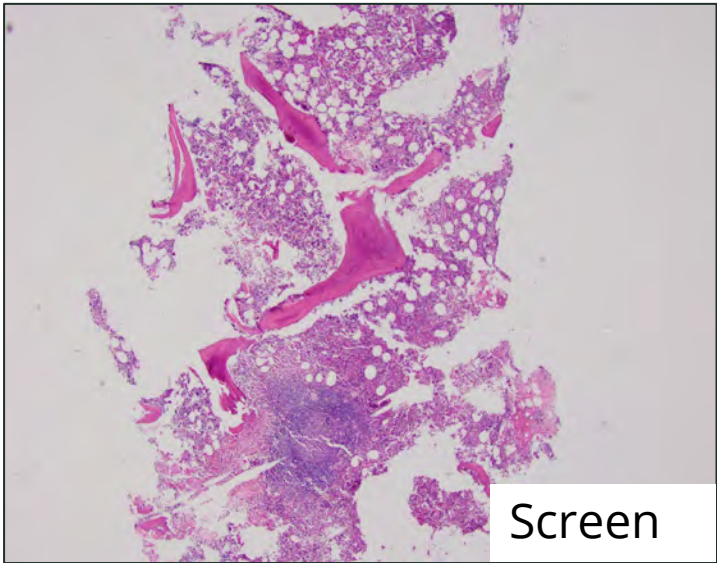
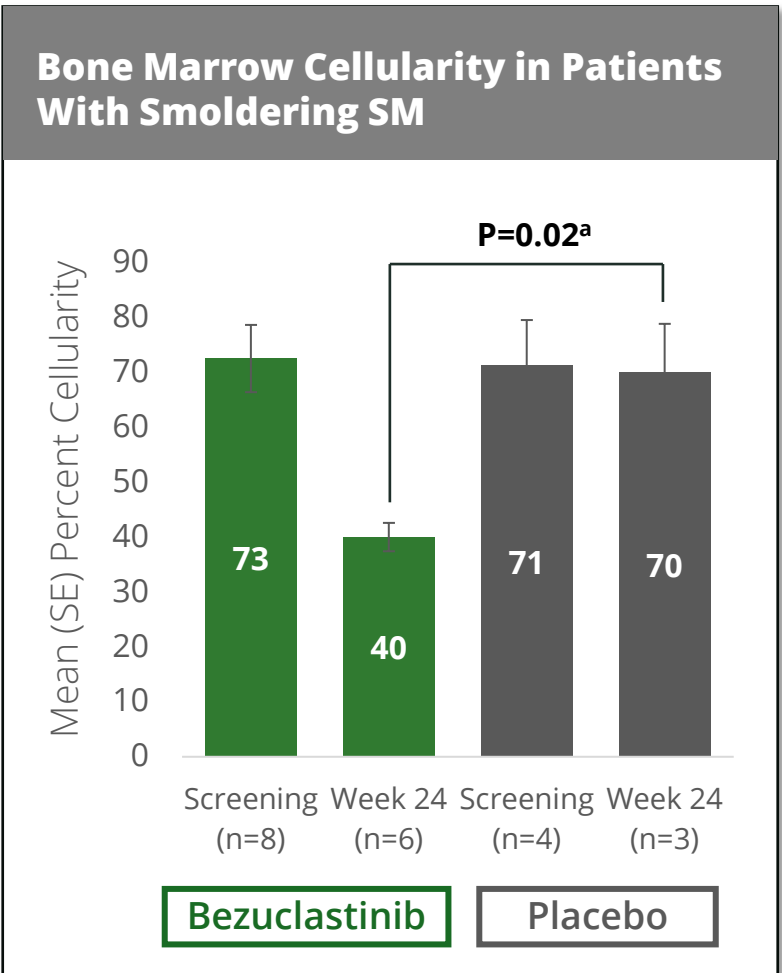
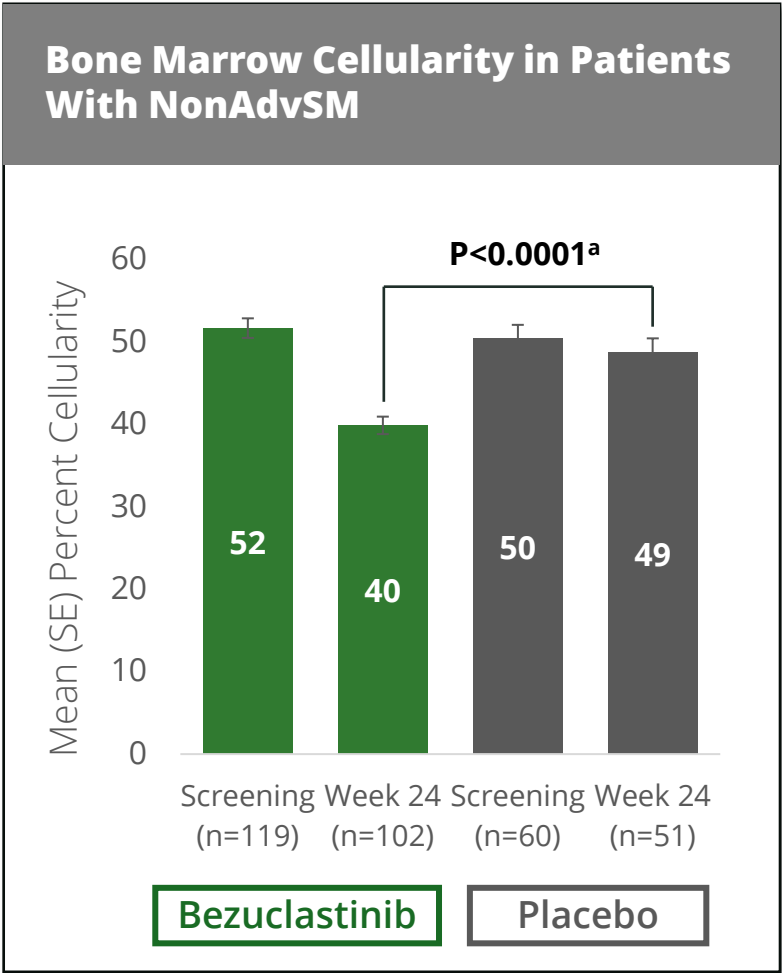
	Bezuclastinib 100 mg QD (N=100*)	Placebo (N=50*)
Mean % of MCs with CD25 expression		
Baseline	89%	87%
24 weeks	23%	93%
Mean % of MCs with CD30 expression		
Baseline	13%	12%
24 weeks	3%	16%

^a P-value is calculated with a two sample t-test of change from baseline in bezuclastinib vs. placebo. $P < 0.0001$ for both CD25 and CD30. Data cutoff: May 22, 2025

Bezuclastinib Reduced Bone Marrow Mast Cell Burden and Aberrant Expression of CD25



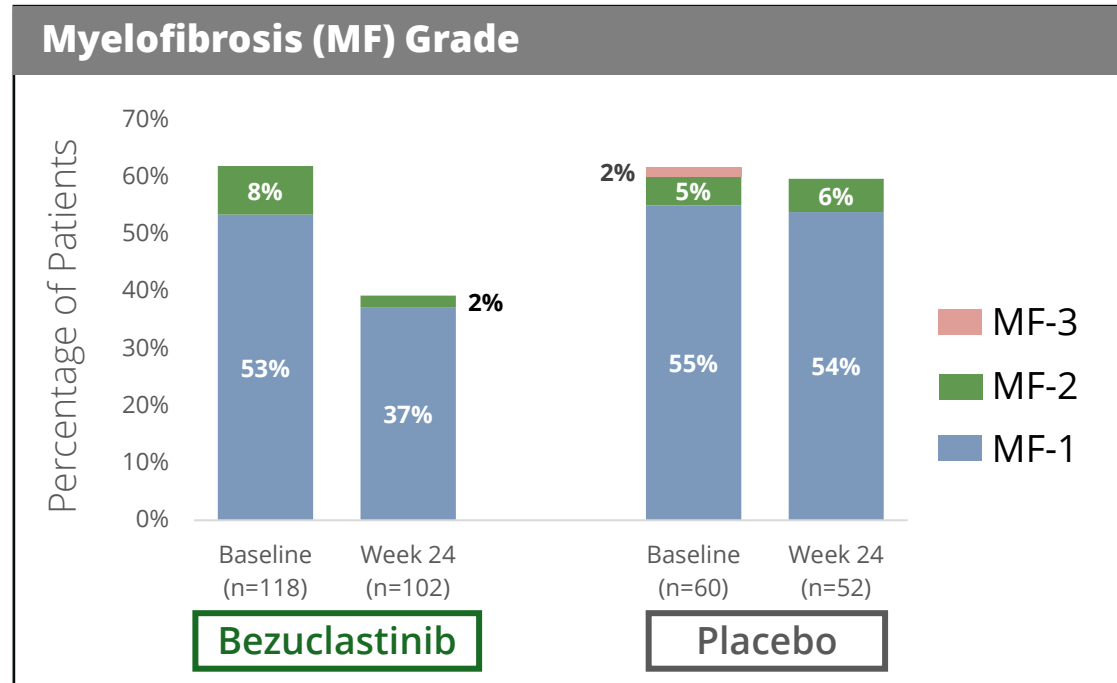
Bezuclastinib Demonstrated Statistically Significant Bone Marrow Cellularity Reduction Overall and in Patients With Smoldering SM



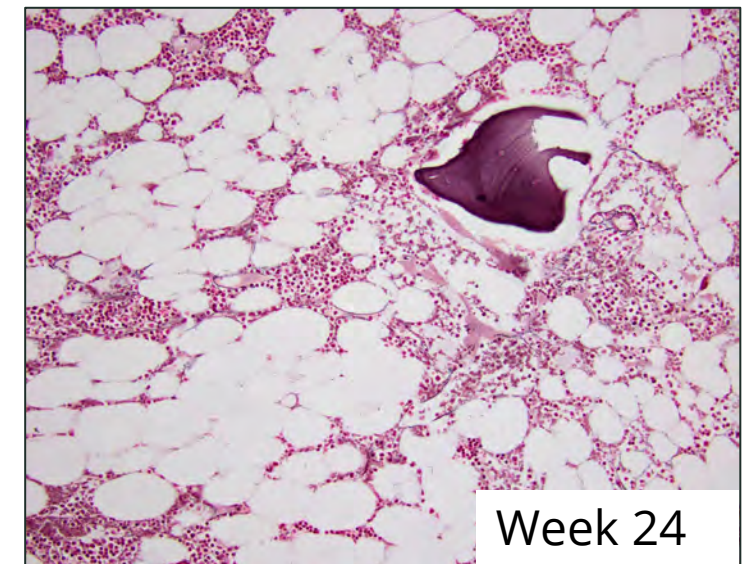
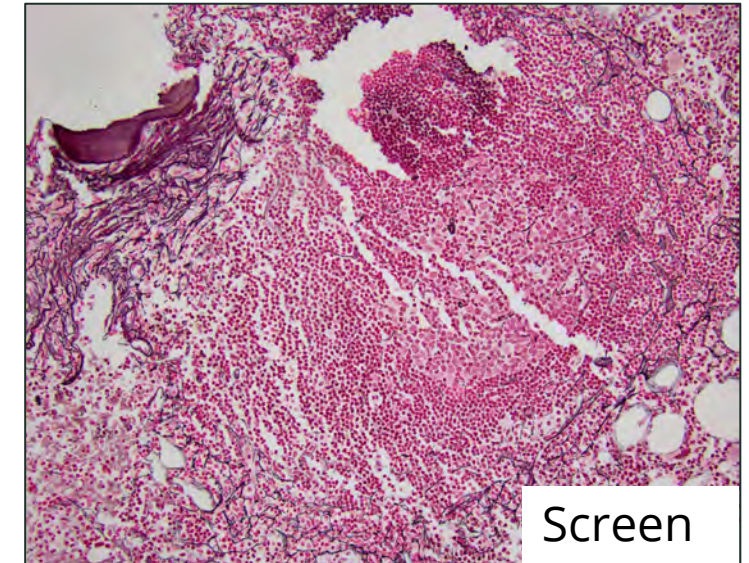
H&E

^a P-value is calculated with a two sample t-test of change from baseline in bezuclastinib vs. placebo
Data cutoff: May 22, 2025.

Bezuclastinib Treatment Led to Improvement in Myelofibrosis Grade at 24 Weeks



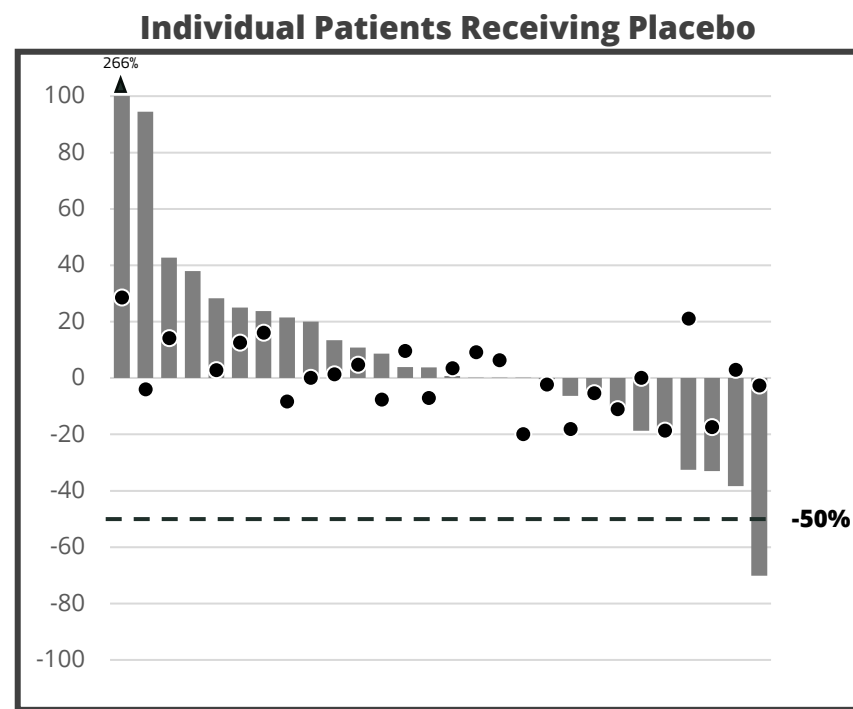
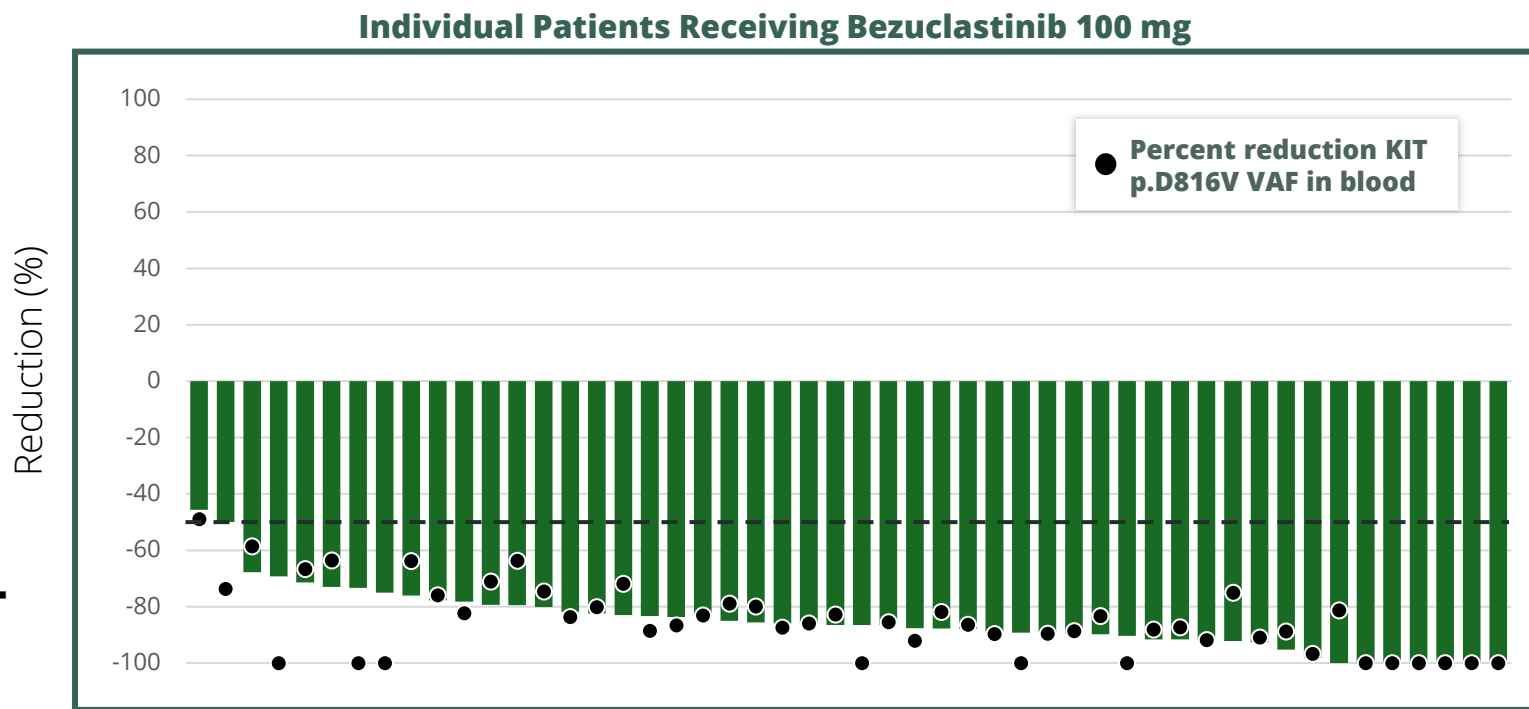
- Percentage of patients with any myelofibrosis grade decreased from 62% at baseline to 39% after 24 weeks of bezuclastinib treatment, while placebo group remains largely unchanged.
- Reduction in myelofibrosis grade may indicate potential disease-modifying activity, particularly in patients with higher-risk systemic mastocytosis



Reticulin

Bezuclastinib Reduced KIT p.D816V VAF in Blood and Bone Marrow

KIT p.D816V VAF in Bone Marrow

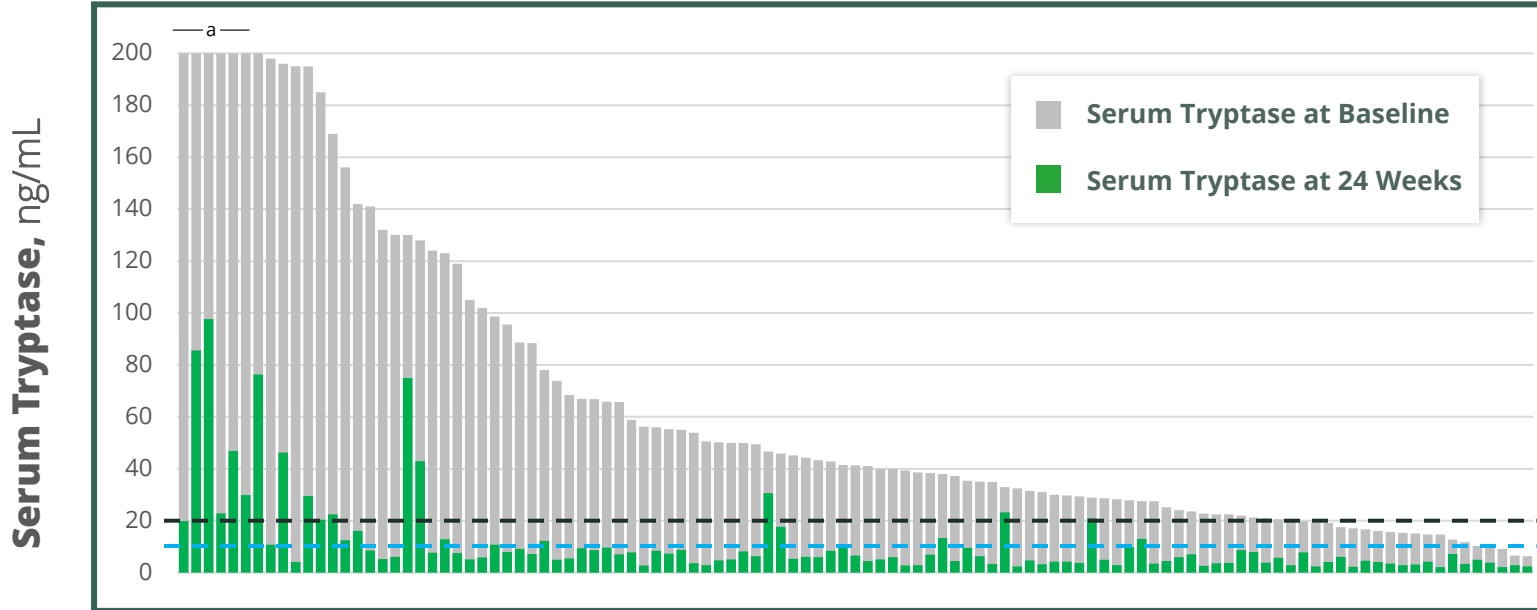


- 62/64 (97%) achieved $\geq 50\%$ reduction or became undetectable in bone marrow at Week 24 versus 1/33 (3%) on placebo; 19/64 (30%) vs 0 on placebo achieved undetectable^a levels of the mutation.
- These bone marrow KIT p.D816V VAF results are consistent with reductions observed in peripheral blood, reinforcing strong disease-modifying potential.

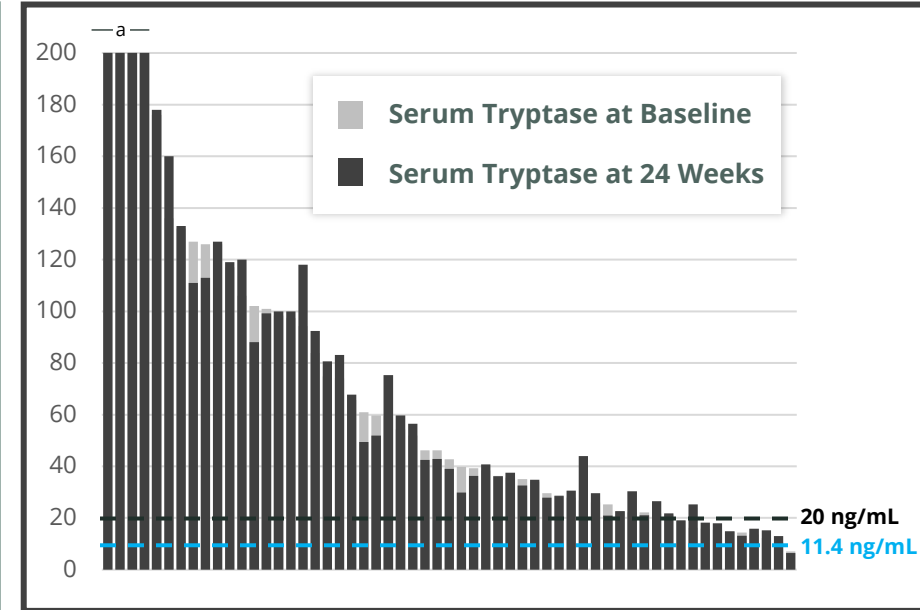
^aLimit of detection equals 0.03%.
Data cutoff: May 22, 2025.
VAF, variant allele frequency.

Bezuclastinib Reduced Serum Tryptase to Normal Levels in Patients With NonAdvSM

Individual Patients Receiving Bezuclastinib 100 mg



Individual Patients Receiving Placebo

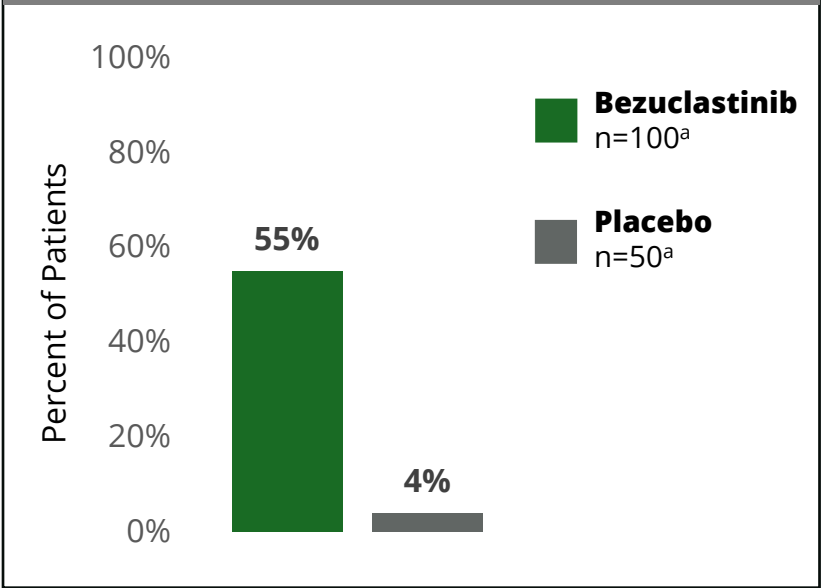


- Among 89 bezuclastinib treated patients with elevated serum tryptase of ≥ 20 ng/mL at baseline, 74 (83%) achieved normalization to < 20 ng/mL after 24 weeks of bezuclastinib treatment.
- Among 104 bezuclastinib treated patients with elevated serum tryptase of ≥ 11.4 ng/mL at baseline, 81 (78%) achieved normalization to < 11.4 ng/mL after 24 weeks of bezuclastinib treatment.

^aPatients exceeding 200 ng/mL serum tryptase.
Data cutoff: May 22, 2025.

55% of Patients Receiving Bezuclastinib No Longer Meet WHO Diagnostic Criteria and 91% Achieve Pure Pathologic Response

Percent of Patients Not Meeting WHO Diagnostic Criteria at 24 Weeks of Treatment



Percent of Patients with Exploratory Pure Pathologic Response¹ (PPR) at 24 Weeks of Treatment

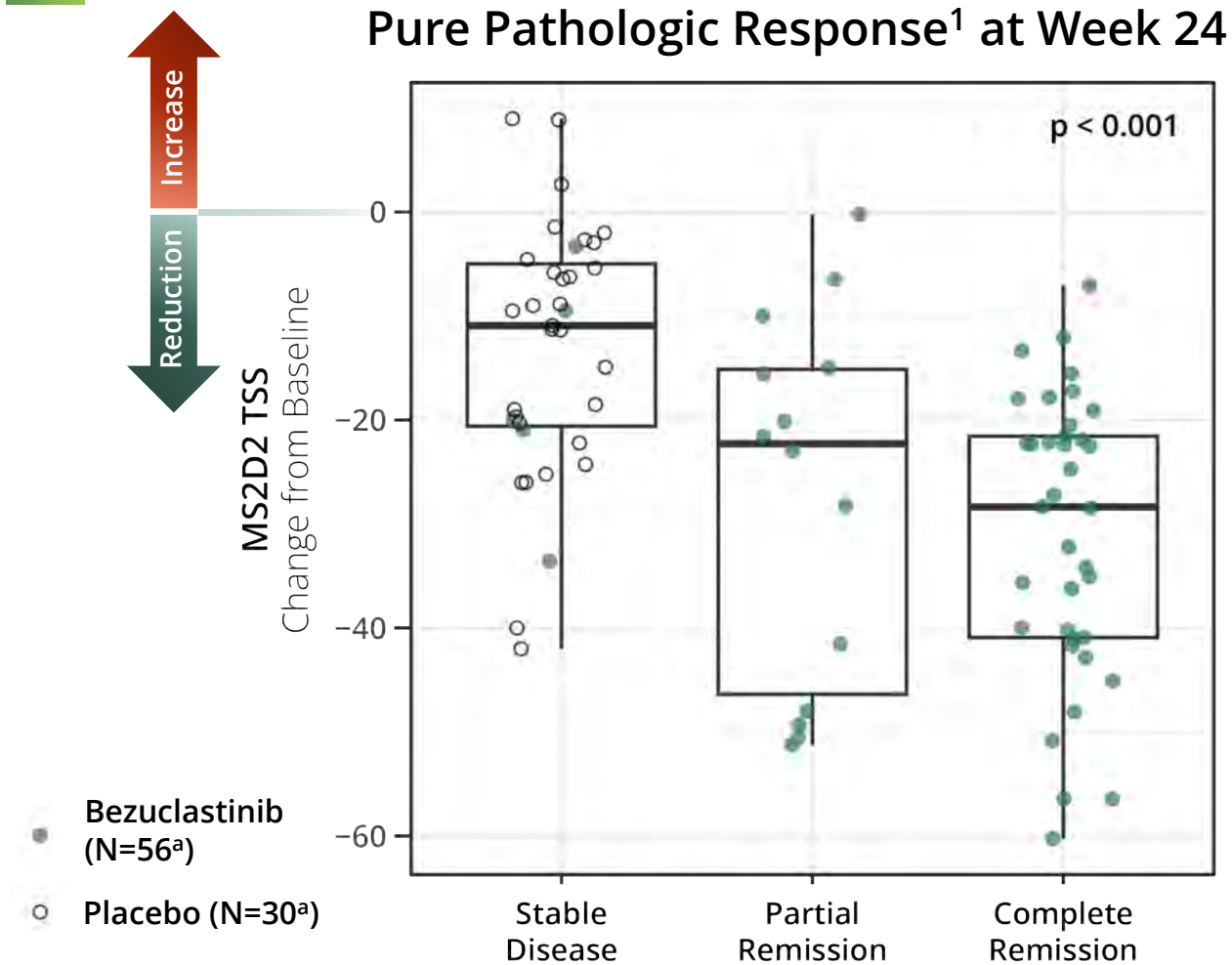
Evaluable Population ^b	Bezuclastinib N=57	Placebo N=31
Overall Response Rate Either Complete or Partial Remission	91% (52)	0% (0)
• Complete Remission (CR) Clearance of aggregates, serum tryptase ≤20 ng/mL, and full or partial hematologic recovery	67% (38)	0% (0)
• Partial Remission (PR) 50% reduction in MC burden and serum tryptase	25% (14)	0% (0)
Stable Disease (SD) Not meeting criteria for PR or CR	9% (5)	100% (31)

- Exploratory analyses of WHO Diagnostic and Pure Pathologic Response Criteria at 24 weeks indicate evidence of disease modification

^aPatients missing data required for SM diagnosis at 24 weeks were excluded. ^bEvaluable patients are defined as those with bone marrow MC aggregates, a positive KIT blood result, and serum tryptase >20ng/mL at baseline and non-missing evaluable response at Cycle 7

1. Shomali et al. *Int J Mol Sci.* 2021; 22(6).

Exploratory Analysis Demonstrated That Pure Pathologic Response (PPR) Correlates With Symptom Improvement



Categories of Pure Pathologic Response

Complete Remission (CR)

Clearance of aggregates, serum tryptase ≤ 20 ng/mL, and full or partial hematologic recovery

Partial Remission (PR)

50% reduction in MC burden and serum tryptase

Stable Disease (SD)

Not meeting criteria for PR or CR

^aEvaluable patients are defined as those with bone marrow MC aggregates, a positive KIT blood result, and serum tryptase >20 ng/mL at baseline and non-missing evaluable response at Cycle 7

1. Shomali et al. *Int J Mol Sci*. 2021; 22(6).

Data cutoff: May 22, 2025.

Bezuclastinib Achieves Reversal of SM Diagnostic Criteria and Normalization of MC Phenotype, Establishing a New Benchmark in Disease Modification for NonAdvSM

Bezuclastinib treatment reversed key bone marrow pathology in NonAdvSM

- Dense mast cell aggregates reduced dramatically from 74% to 13%, eliminating the major WHO diagnostic criterion.
- Bone marrow mast cells decreased from 18% to 5%, with atypical morphology reduced by 28%.
- Mast cell phenotype normalized, with deep reductions in CD25 and CD30 expression.

The effects observed in bone marrow corresponded to pathologic response and a resolution of diagnostic criteria.

- By Week 24, 55% of patients on bezuclastinib no longer met WHO SM diagnostic criteria, compared to 4% patients on placebo.
- Pure pathologic response was achieved in 91% of bezuclastinib-treated patients versus 0% on placebo, and pure pathologic response strongly correlated with symptom improvement.