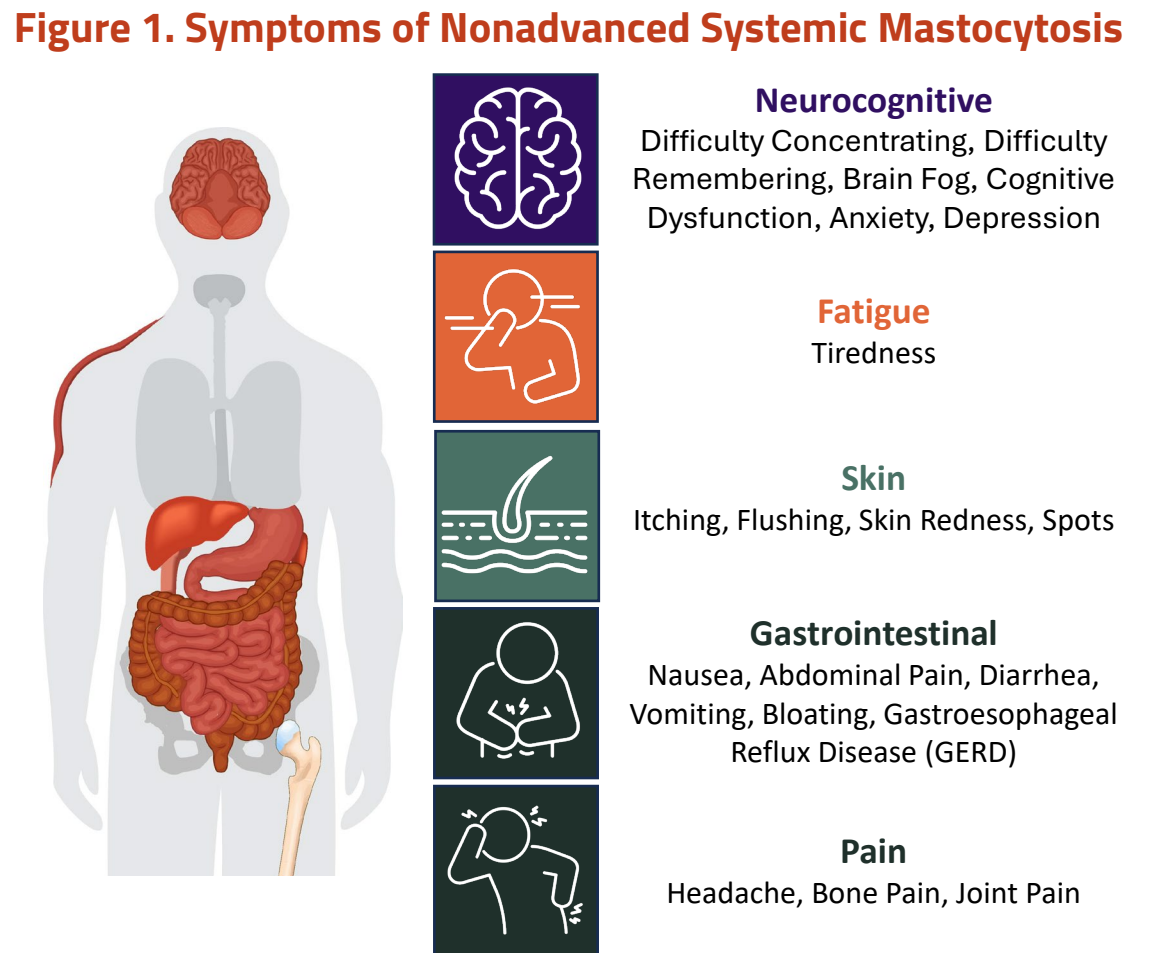


INTRODUCTION

Systemic Mastocytosis (SM) is a Rare and Debilitating Disease Characterized by Neoplastic Mast Cell Infiltration of Extracutaneous Tissues and Symptoms of Mast Cell Activation¹

- Nonadvanced SM (NonAdvSM)² includes indolent SM (ISM) as well as smoldering SM (SSM),³ for which no disease-modifying therapies are approved.
- Patients with NonAdvSM experience a variety of disabling, potentially serious and severe symptoms which may significantly reduce health-related quality of life. Symptoms are caused by mast cell reactions and can include life-threatening anaphylaxis.⁴
- Agents targeting *KIT* D816V are used to treat Advanced SM (AdvSM) and NonAdvSM, but unmet need remains.⁵⁻⁷
 - AEs like cognitive impairment, bleeding, and edema can limit dosing of other agents, resulting in poor symptom control.



Bezuclastinib is an Oral, Potent, and Selective Type 1 Tyrosine Kinase Inhibitor (TKI) With Activity Against *KIT* D816V and An Encouraging Safety and Tolerability Profile

- Summit Part 1 Goals:**
- Determine recommended dose of bezuclastinib based on safety, PK, and PD.
 - Explore the effects of bezuclastinib on the signs and symptoms of NonAdvSM.
 - Includes assessment of disease-specific symptom severity using a novel patient-reported outcome measure, the Mastocytosis Symptom Severity Daily Diary (MS2D2).
- Results After 12 Weeks of Bezuclastinib Treatment in Summit Part 1:**
- Bezuclastinib demonstrated an encouraging safety and tolerability profile.
 - Patients randomized to 100mg, regardless of formulation, had similar exposure and PK profiles.
 - Mean (SD) steady state AUC_{0-24h} at C2D1: 16,900 (29.2) ng*h/mL in Part 1a and 16,900 (41.2) ng*h/mL in Part 1b.
 - Patients treated with 100mg dose reported significant positive impact on health-related quality of life (HRQoL) measures, skin manifestations, and other symptoms as measured by the MS2D2.⁸
 - Reduction in mast cell burden was robust among patients treated with 100mg dose: 94.4%, 100%, and 92.3% had at least a 50% reduction in basal serum tryptase, KIT p.D816V variant allele frequency, and bone marrow mast cells, respectively.⁹
- Totality of results from Summit Part 1 support 100mg QD (optimized formulation) as the optimal dose of bezuclastinib for Part 2 of the study.¹⁰*

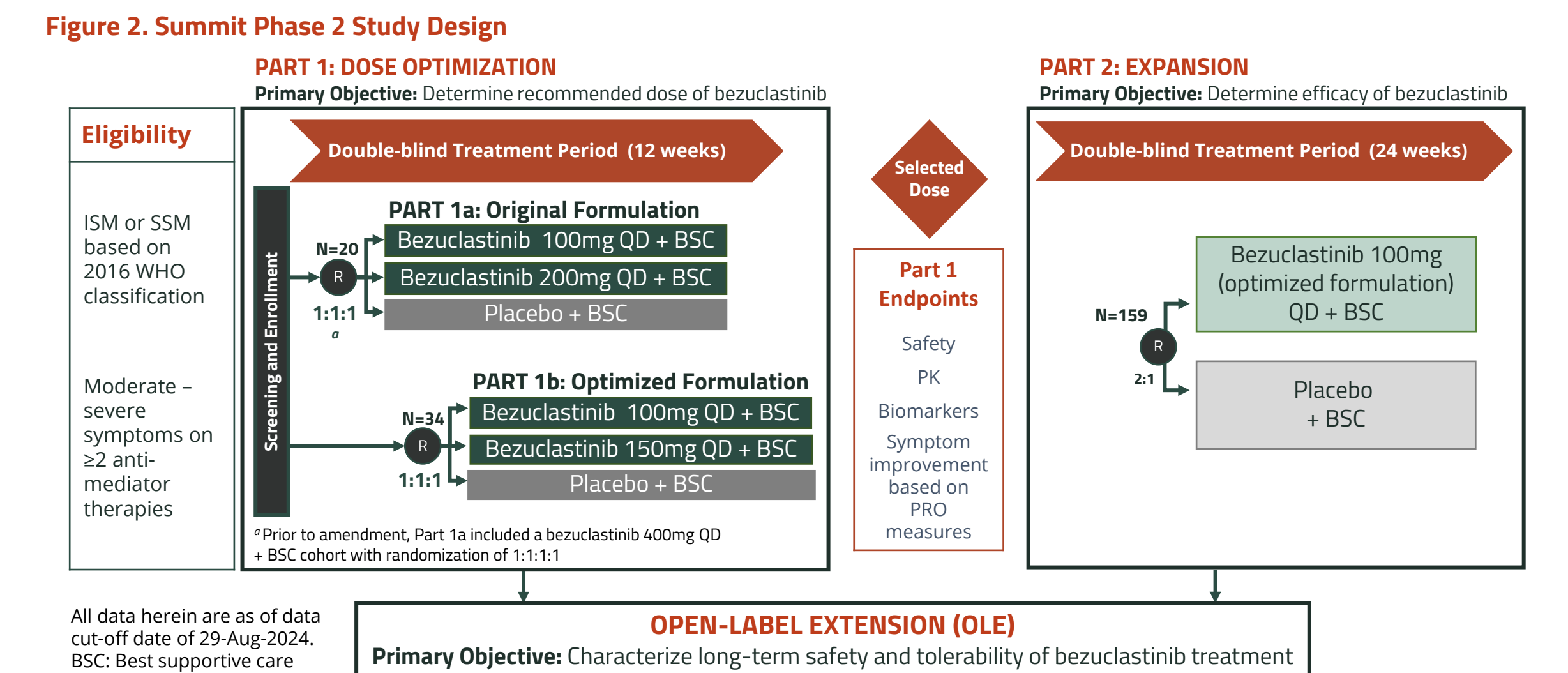
Mastocytosis Symptom Severity Daily Diary (MS2D2) – A Novel Patient-Reported Outcome Measure (PROM) Designed to Assess Disease-Specific Symptom Severity in NonAdvSM Patients

- The MS2D2² is a 17-item measure addressing signs and symptoms of NonAdvSM.
- Eleven symptoms within 4 domains are included in MS2D2 Total Symptom Score (TSS).
 - Severity of each of these symptoms is assessed daily from 0 (none) to 10 (worst possible).
 - TSS is analyzed as a 14-day average.
- Data from Summit Part 1 support MS2D2 as a reliable, valid and “fit-for-purpose” PROM to assess treatment efficacy as the primary endpoint in Summit Part 2.⁹

Table 1. MS2D2 Total Symptom Score (TSS) Domains and Symptoms

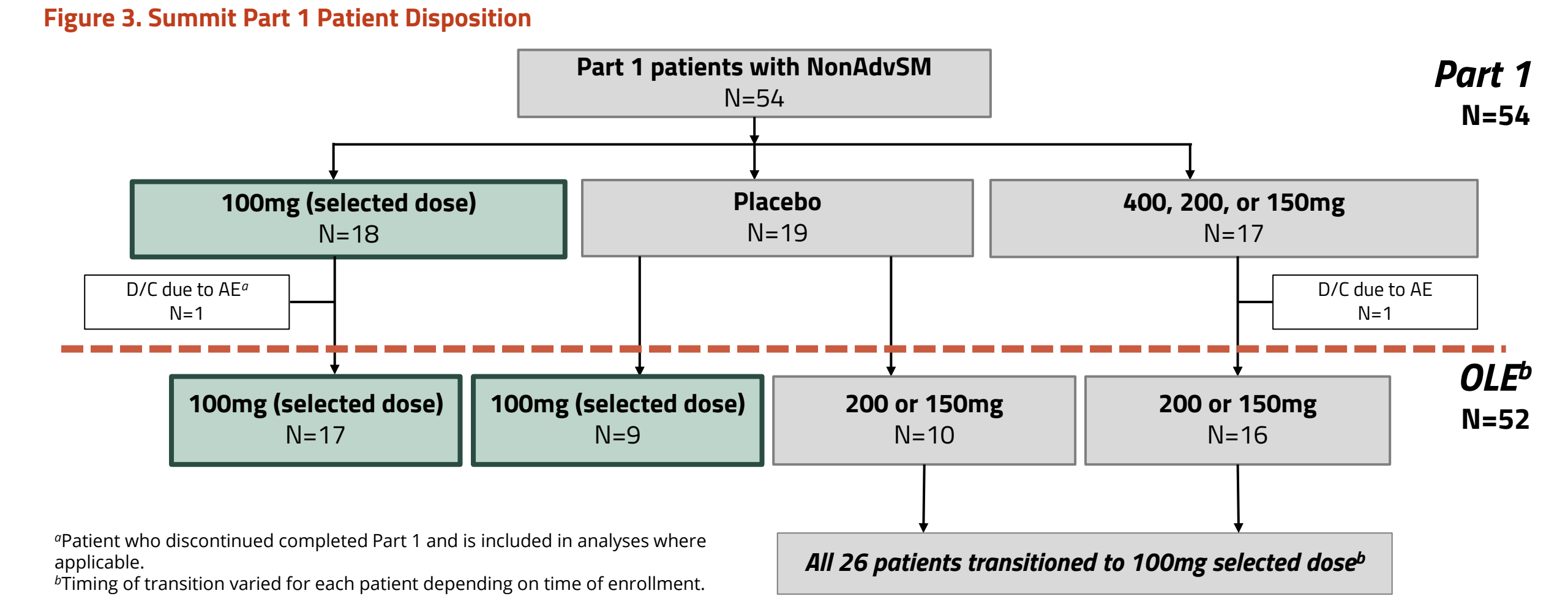
Domain	Symptom
Neurocognitive	Concentration, Remembering
Fatigue	Tiredness
Skin	Itching, Flushing, Skin redness, Spots
Other	Gastrointestinal (Nausea, Abdominal pain), Pain (Headache, Bone pain)

Summit (NCT05186753): Phase 2 Double-Blind, Placebo-Controlled Randomized Clinical Study Evaluating Bezuclastinib in NonAdvSM

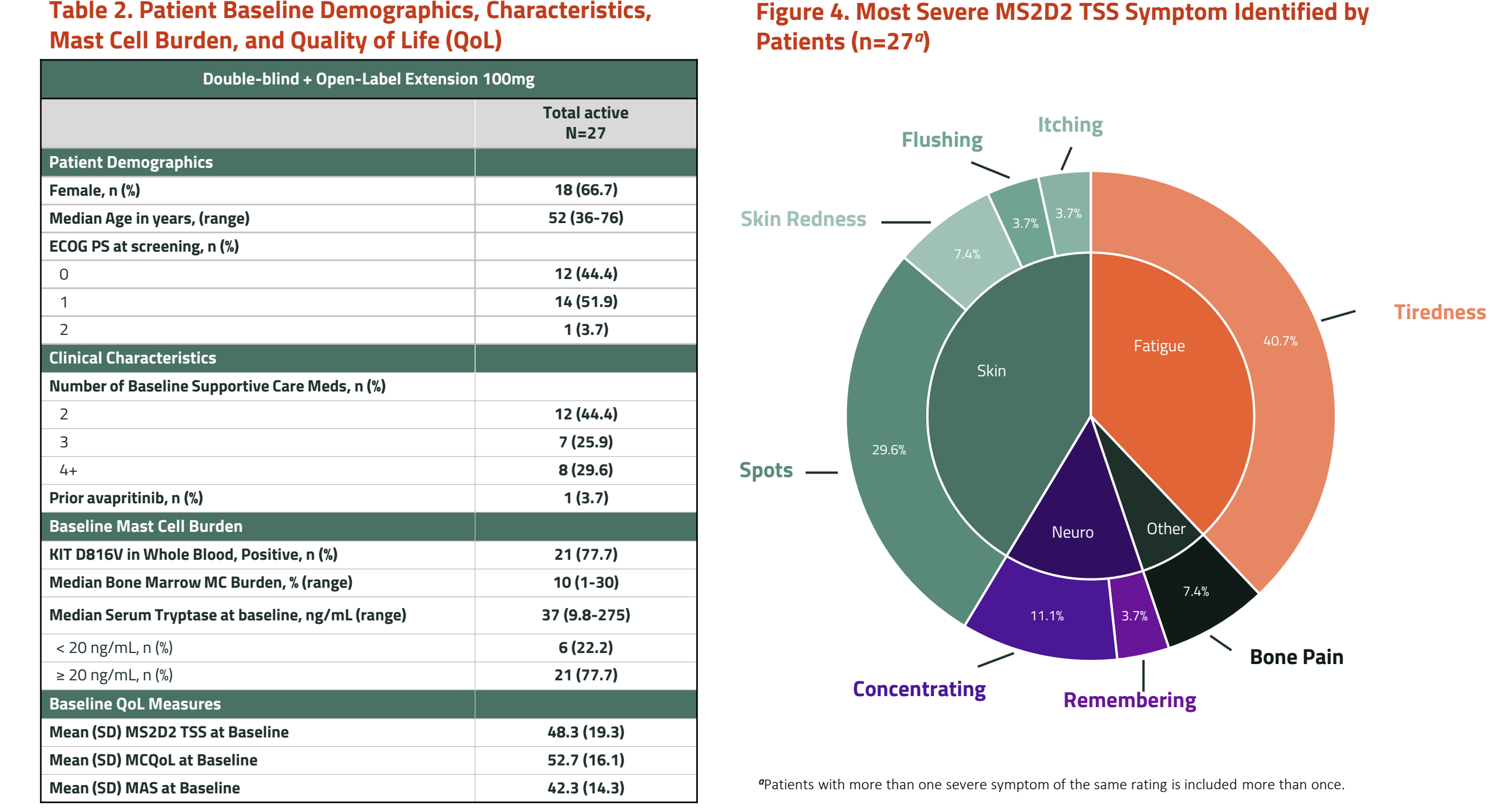


RESULTS

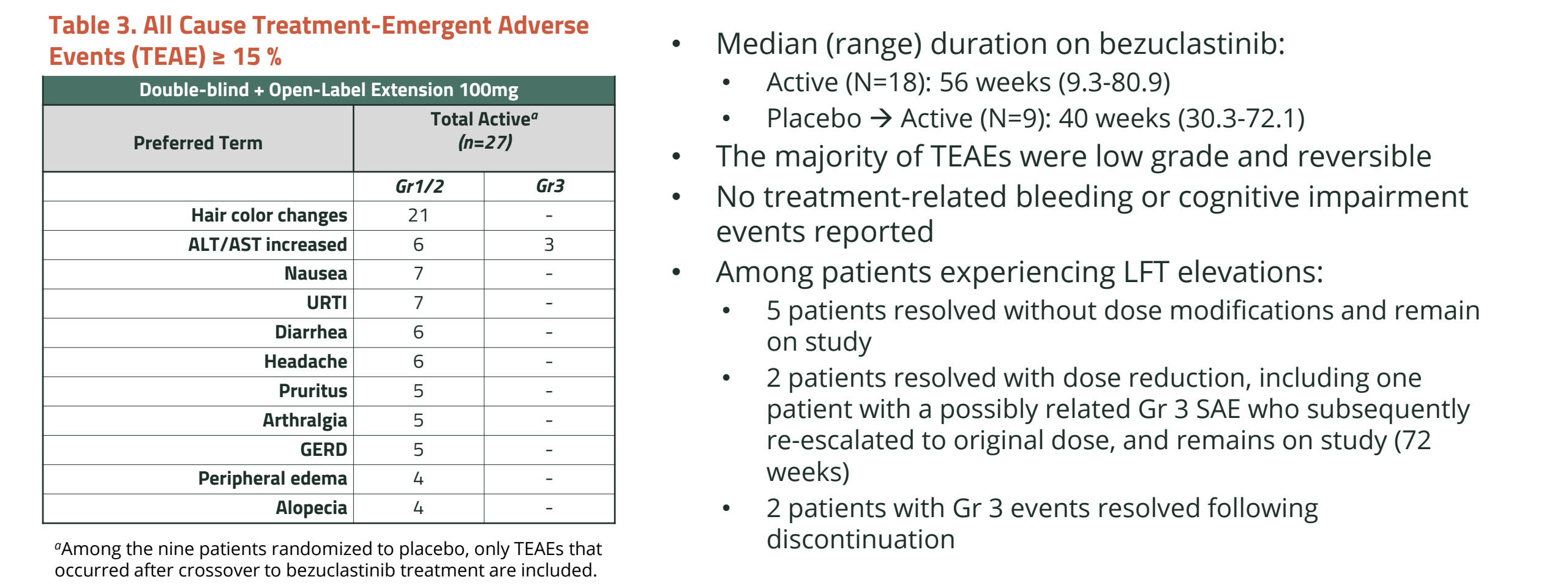
Disposition for Part 1 Patients Receiving the Selected Dose of 100mg QD Bezuclastinib



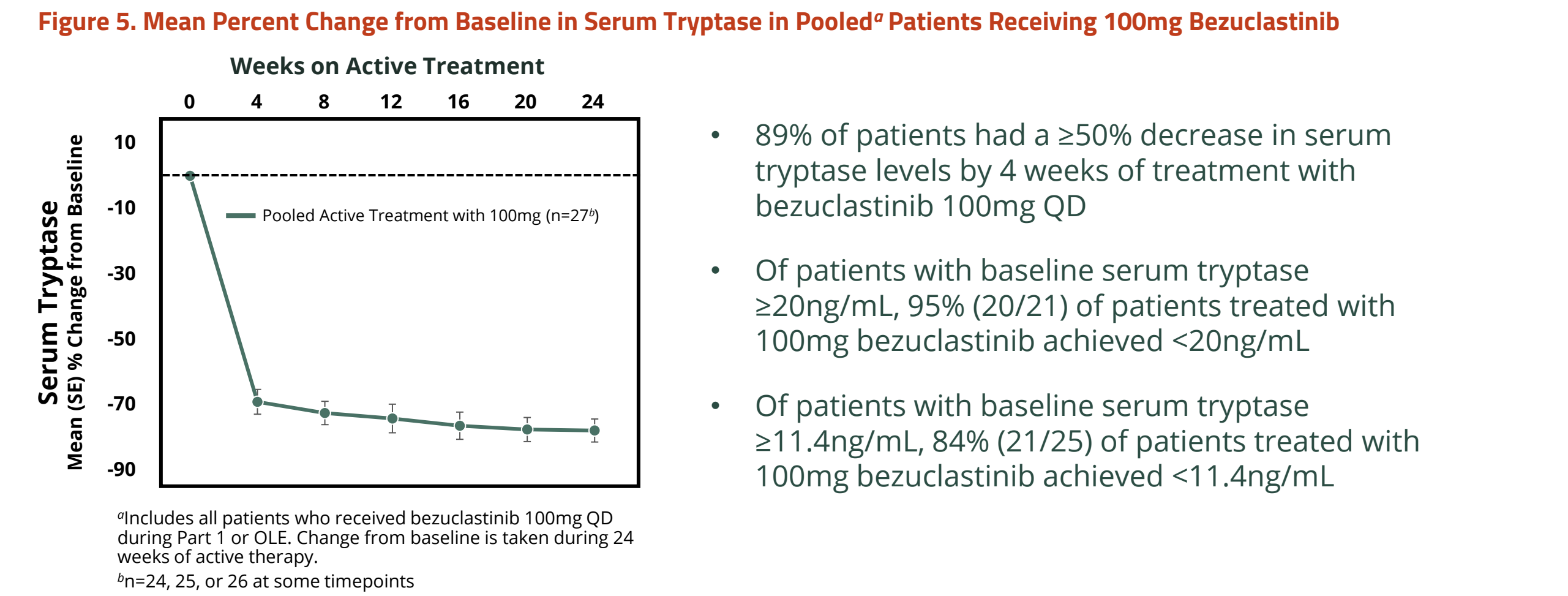
Part 1 – All NonAdvSM Patients with Moderate to Severe Disease and Only Treated with 100mg or Placebo



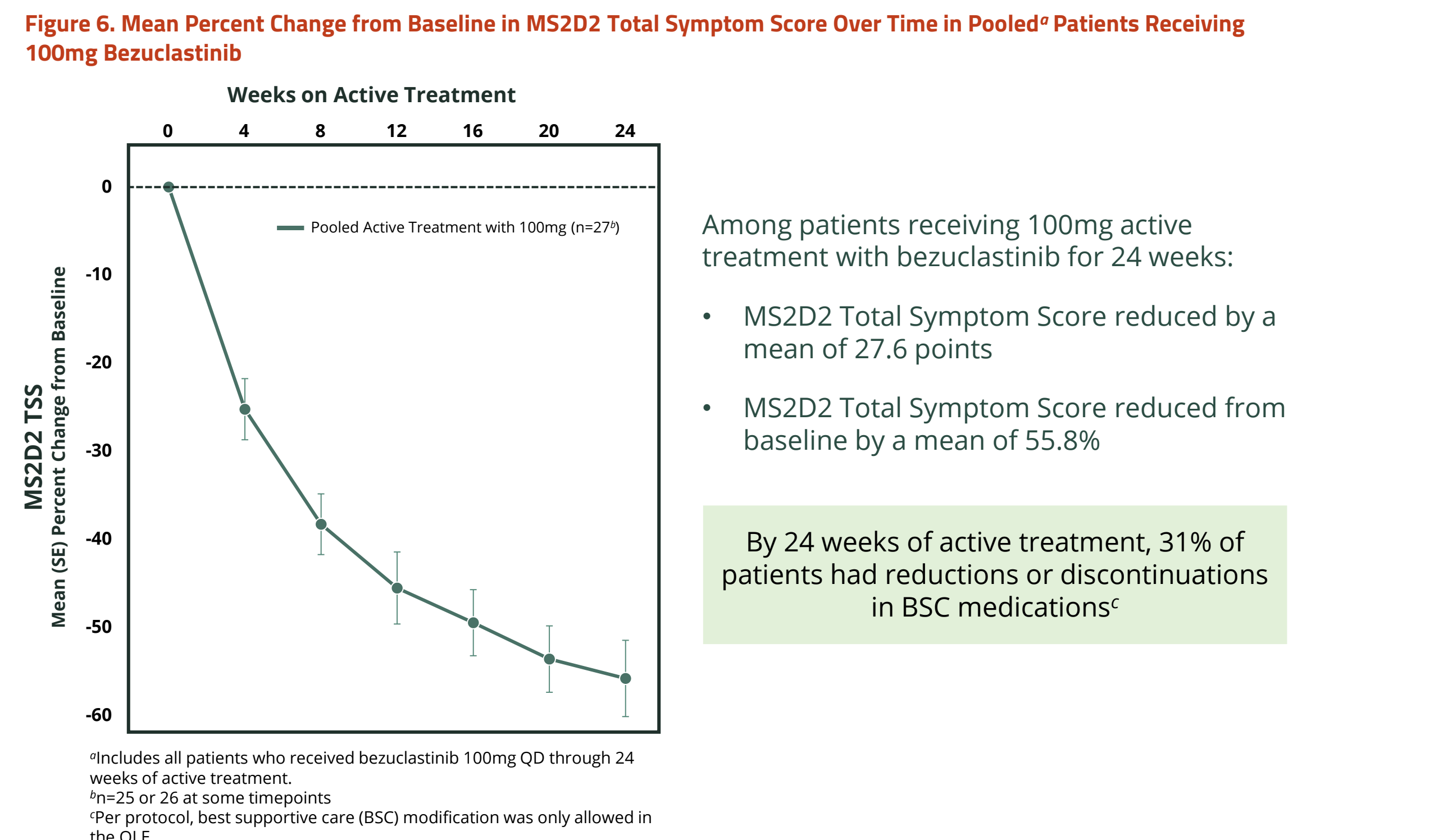
Safety and Tolerability in Patients Randomized to 100mg in Part 1 + OLE



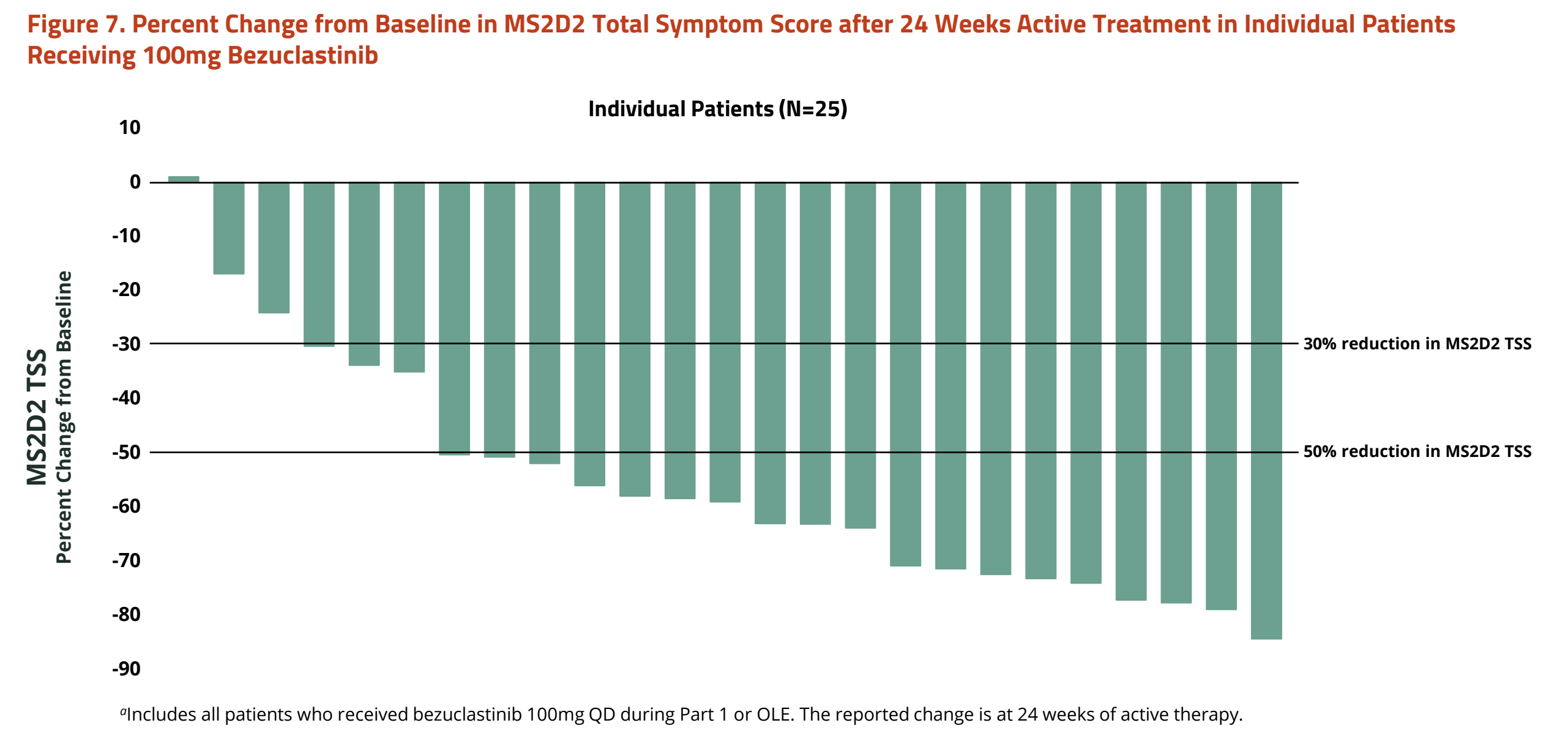
Bezuclastinib 100mg Led to Rapid, Deep, and Sustained Reductions in Serum Tryptase Over the Course of 24 Weeks of Treatment



Patients Receiving Bezuclastinib 100mg in Part 1 + OLE Reported Sustained Improvements in Symptom Severity

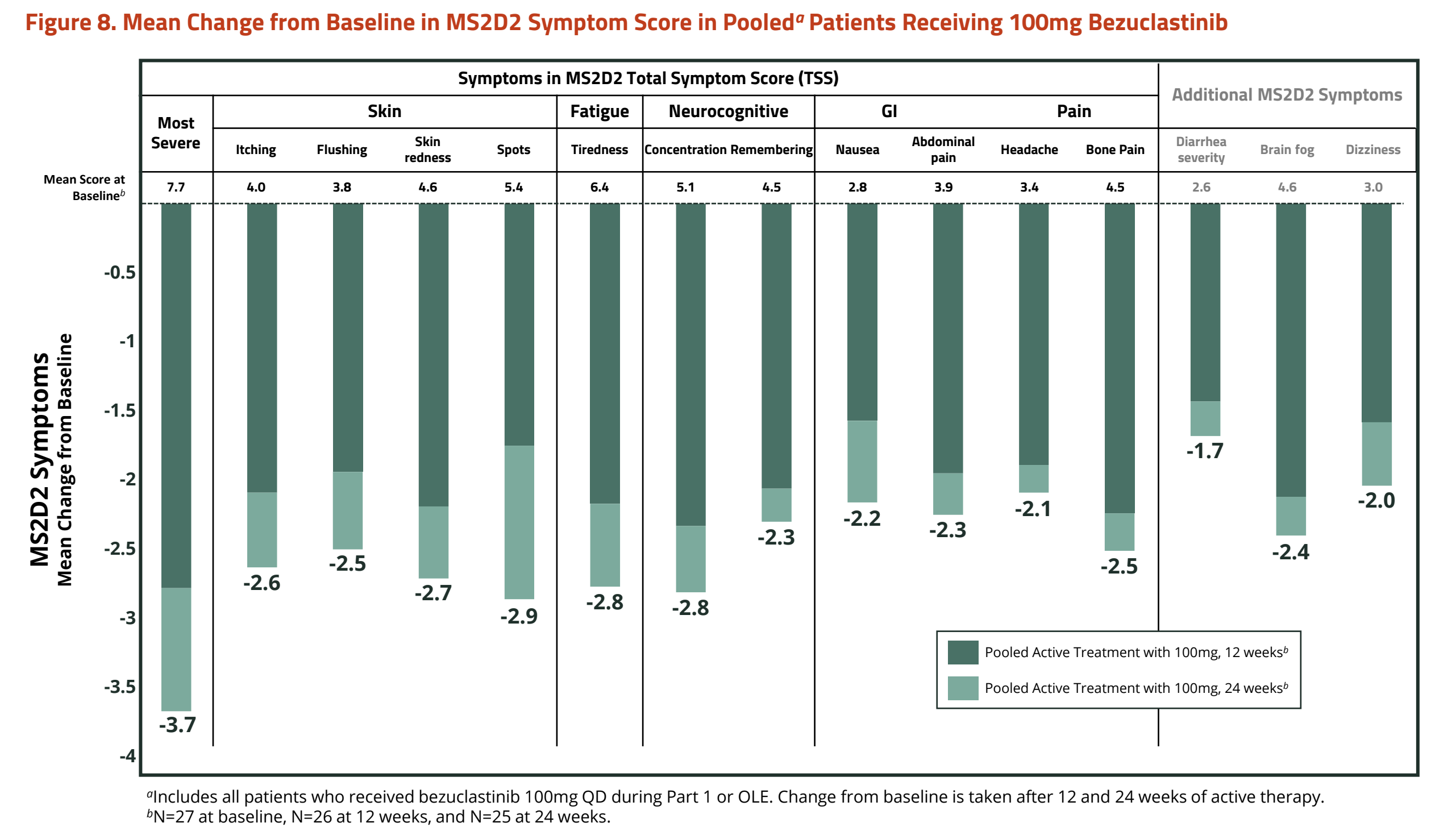


Bezuclastinib 100mg in Part 1 + OLE Showed Significant Clinical Improvements in Symptoms of Non-Advanced SM

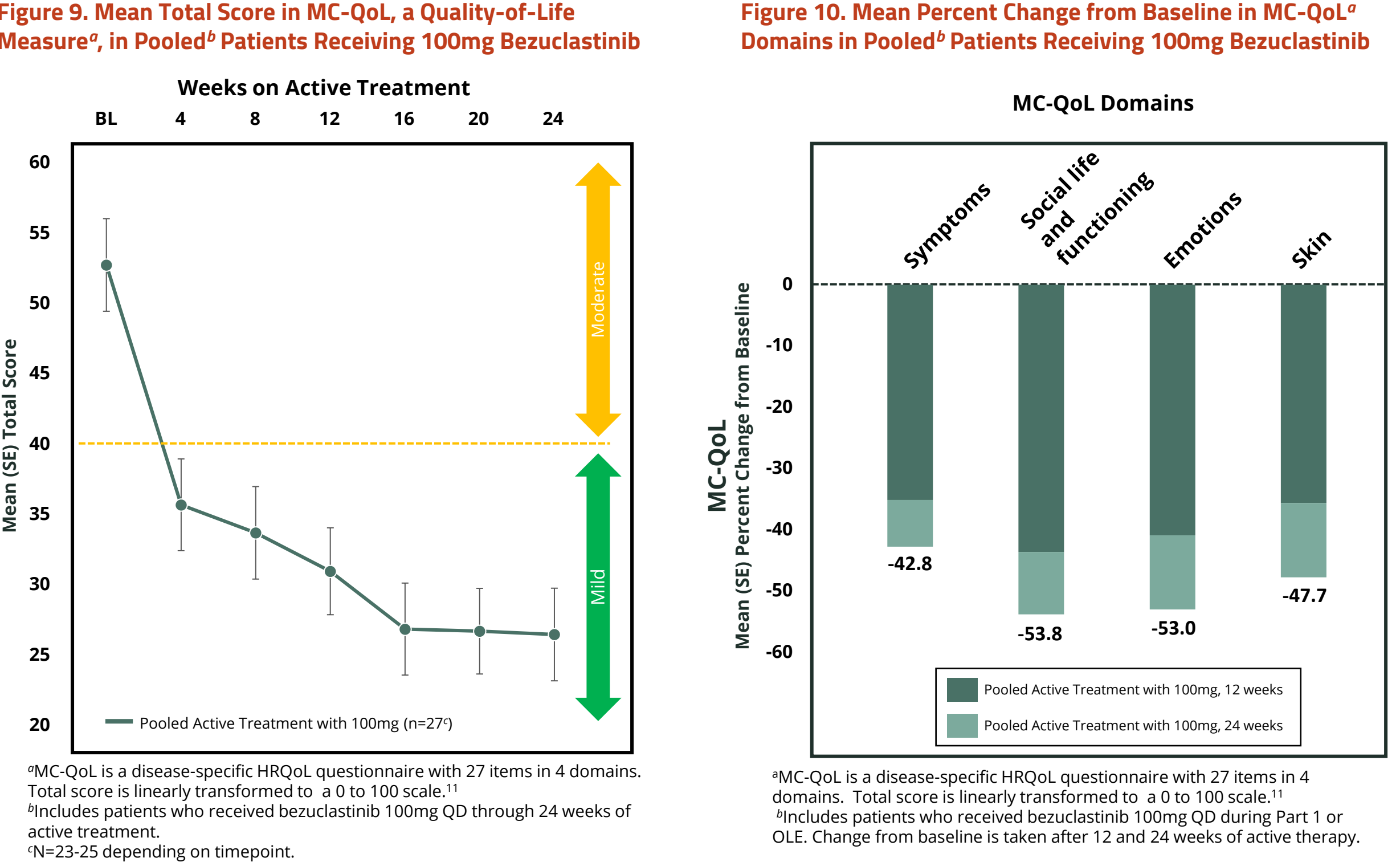


- Among patients receiving 100mg active treatment with bezuclastinib for 24 weeks:
- 88% of patients reached at least 30% reduction in MS2D2 TSS
 - 76% of patients reached at least 50% reduction in MS2D2 TSS

Patients Receiving Bezuclastinib 100mg Demonstrated Clinically Meaningful Changes in Symptoms that Deepened with 24 Weeks of Treatment



Deepening of Health-related QoL Improvements Were Observed in MC-QoL Total Score and Across All MC-QoL Domains During 24 Weeks of Treatment With 100mg Bezuclastinib



- Patients receiving 100mg bezuclastinib had significant improvement in quality of life with a reduction from 'moderate' to 'mild' disease
 - Among patients receiving 100mg active treatment with bezuclastinib for 24 weeks, MC-QoL Total Score reduced by an average of 25.4 points
 - Among patients receiving 100mg active treatment with bezuclastinib for 24 weeks, MC-QoL Total Score reduced from baseline by an average of 48.9%
- Significant improvement in symptoms, social life and functioning, emotions, and skin were reported by patients after 12 and 24 weeks of treatment with bezuclastinib 100mg
 - Among patients receiving 100mg active treatment with bezuclastinib for 24 weeks, Social Life and Functioning improved from baseline, with a > 50% reduction in burden based on MC-QoL

CONCLUSIONS

Data From Part 1+OLE of Summit Demonstrated that 100mg Bezuclastinib is Safe and Led to Robust Improvements in Symptoms and Biomarkers of Mast Cell Burden in Patients with NonAdvSM

- Favorable safety and tolerability profile with continued treatment to 24 weeks:
 - The majority of TEAEs were low grade and reversible
 - No treatment-related bleeding or cognitive impairment AEs reported
- Rapid and sustained reductions in symptom severity based on MS2D2 and MC-QoL measures and objective biomarkers of NonAdvSM:
 - 76% and 88% of patients treated with 100mg achieved at least a 50% and 30% reduction in total symptom severity at Week 24, respectively
 - Substantial reduction in the patients' most severe symptoms at 12 weeks with continued improvement at 24 weeks
 - Clinically significant, deep reductions across all symptoms within MS2D2 that are sustained for 24 weeks
 - 89% of patients had a ≥50% decrease in serum tryptase levels by 4 weeks which was sustained through 24 weeks
 - After 24 weeks, 31% of patients had reductions or discontinuations of BSC medications

Summit Part 2 has completed enrollment ahead of schedule.

ACKNOWLEDGEMENTS:
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