

Symptom and Quality of Life Burden in Patients with Indolent Systemic Mastocytosis

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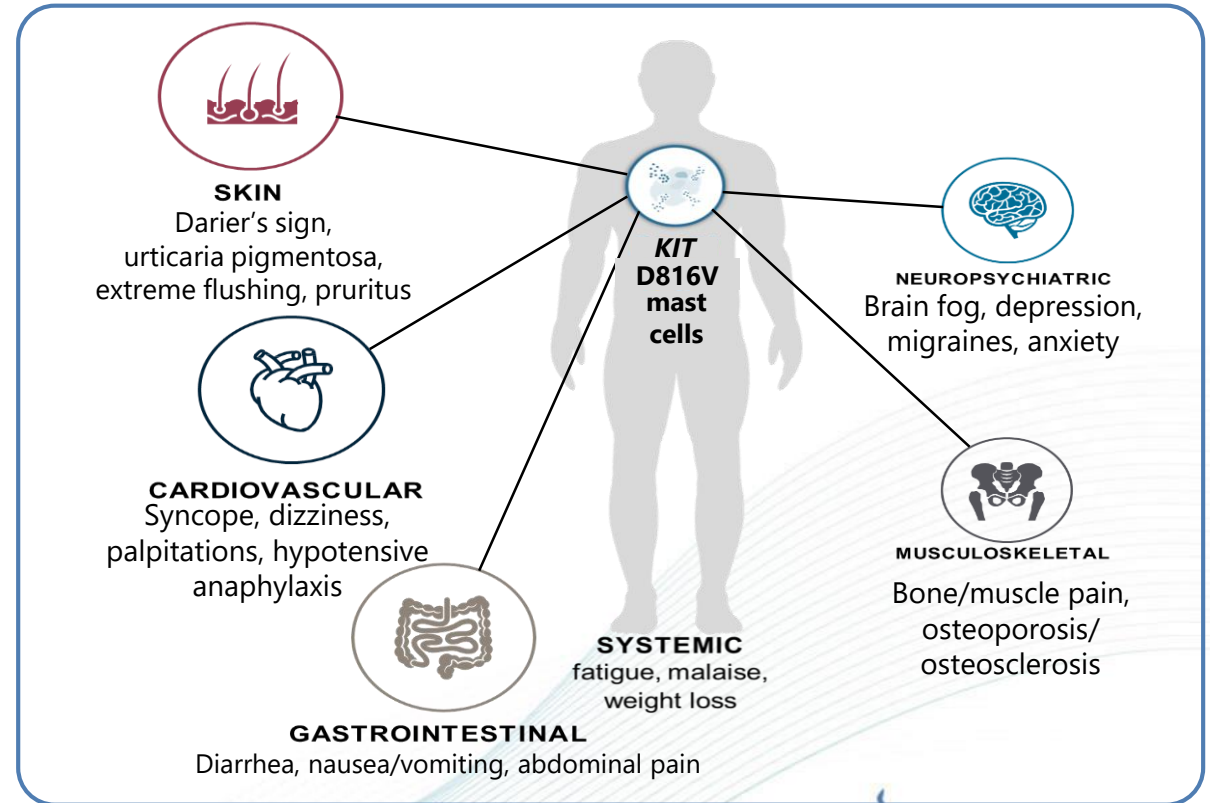
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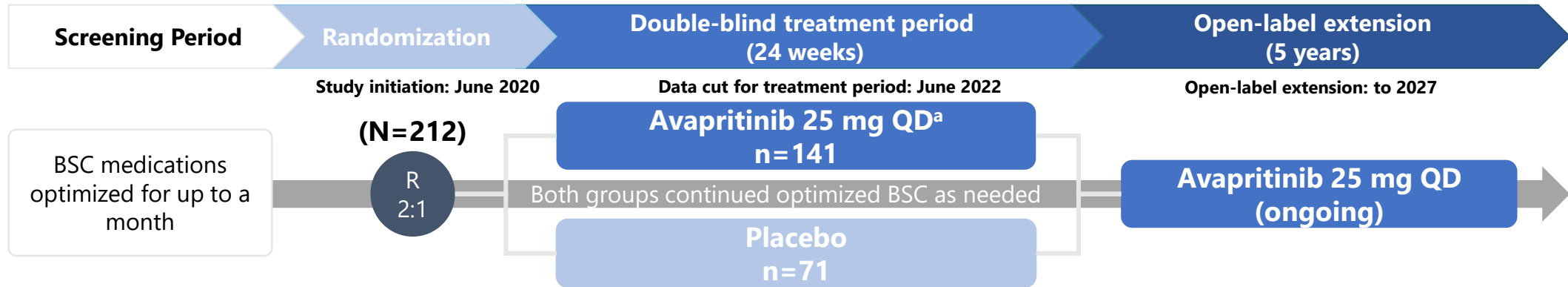
Indolent Systemic Mastocytosis (ISM) Is a Rare, Clonal Disease Primarily Driven by the KIT D816V Gene Mutation In ~95% Of Adult Cases¹⁻³

Patients with ISM experience significant impairment in daily physical functioning and emotional well-being due to severe gastrointestinal, cutaneous, and neurocognitive symptoms; fatigue; and potentially life-threatening anaphylaxis.

- These lifelong symptoms impair ISM patient's quality of life.⁴⁻⁸
- Most patients rely on polypharmacy for management of symptoms with best supportive care (BSC) medications.⁸⁻¹⁰
- For many ISM patients, symptoms are not adequately controlled with BSC medications.⁸⁻¹⁰



The Registrational, Randomized, Double-blinded, Placebo-controlled PIONEER Study Is Currently in Open-label Extension (NCT03731260)



Part 2 – Double-blind Treatment Period Endpoints

Primary Endpoint: ISM Symptoms

- Mean change in **ISM-SAF** Total Symptom Score (**TSS**) from baseline to Week 24

Secondary and Exploratory Endpoints:

Individual and Most Severe Symptoms, Biomarkers of Mast Cell Burden, and QoL/Health Status Measures

- Mean change in individual symptom scores of ISM-SAF
- Mean change in most severe symptom score
- $\geq 50\%$ reduction in serum tryptase levels
- $\geq 50\%$ reduction in KIT D816V VAF in peripheral blood
- $\geq 50\%$ reduction in in bone marrow mast cell aggregates
- Mean % change in QoL scores, as measured by **MC-QoL**, **SF-12**, **EQ-5D**, and **PGI-S**

At 24 Weeks, All Primary, Secondary and Exploratory Endpoints Were Positive¹¹

BSC, Best Supportive Care; R, randomized; QD, once daily; ISM-SAF, Indolent Systemic Mastocytosis-Symptom Assessment Form; TSS, total symptom score; QoL, quality of life; VAF, variant allele fraction; MC-QoL, Mastocytosis Quality of Life Questionnaire.

^a The recommended dose of avapritinib for the double-blind period and open-label extension was identified based on efficacy and safety results from Part 1 that included 4 cohorts: 25 mg avapritinib (n=10), 50 mg avapritinib (n=10), 100 mg avapritinib (n=10) and placebo (n=9).



Despite Use of Multiple Symptom-directed Therapies, Patients with ISM Demonstrated High Symptom Burden at Baseline

Baseline Mean(SD) TSS = **50.9 (19.4)**
 ≥ 42 Indicates Severe ISM¹²

Baseline Mean Number of BSC Treatments*
3.8 (Range 0-11)

Mean Age: **49.9**

72.6% Female

Baseline Mean Serum
Tryptase (ug/l)

60.9

Baseline Mean Bone
Marrow Mast Cells (%)

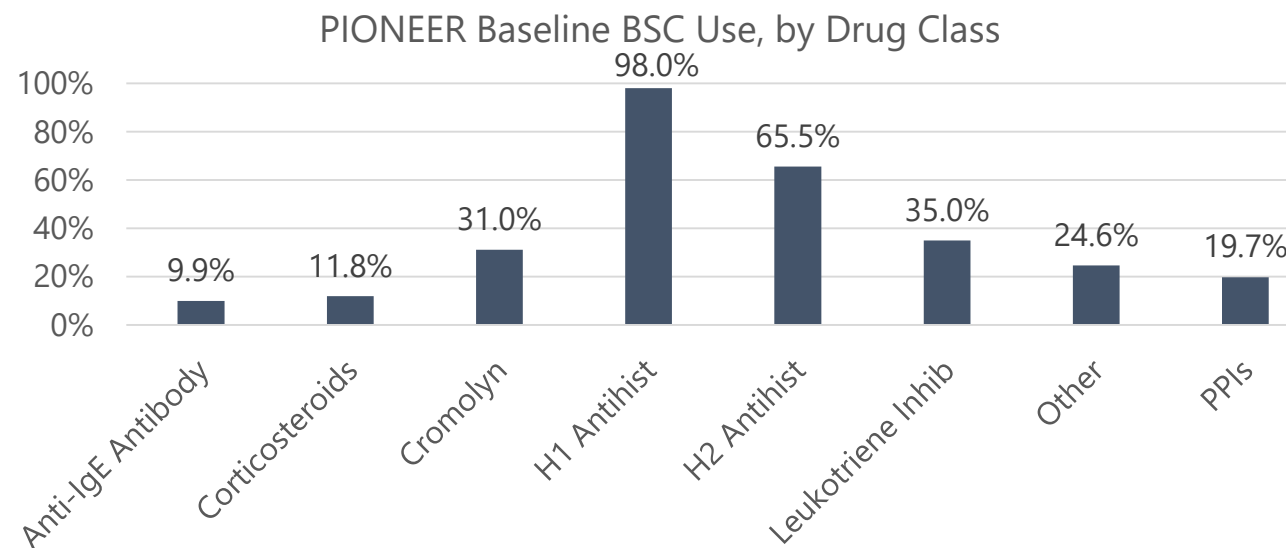
11.4%

Proportion with Baseline
Serum Tryptase ≥ 125
ng/mL**

12.3%

Proportion with Baseline
KIT D816V VAF $\geq 6\%$ **

14.3%



*All patients had at least two BSC prior to or at screening. A total of 15 (7.0%) patients had <2 BSC at the start of the study.

**Based on analysis of 203 evaluable patients in Part 2 double-blind treatment period.

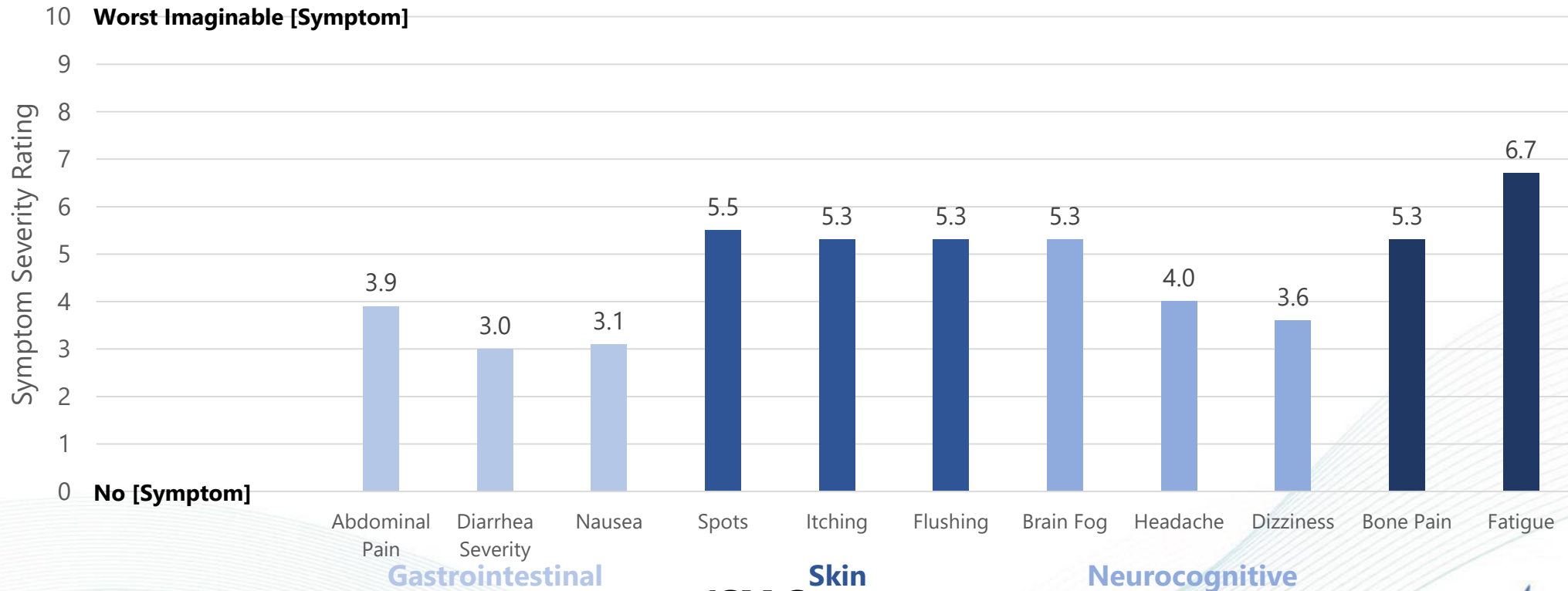
ISM: Indolent Systemic Mastocytosis; SD: Standard Deviation; TSS: Total Symptom Score; VAF: Variant Allele Fraction; BSC: Best Supportive Care; PPI: Proton Pump Inhibitor



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Nearly All PIONEER Patients Reported 7 or More Symptoms at Baseline

Mean Individual Symptom Scores from ISM-SAF at Baseline



98.5%

Reported 7 or more symptoms

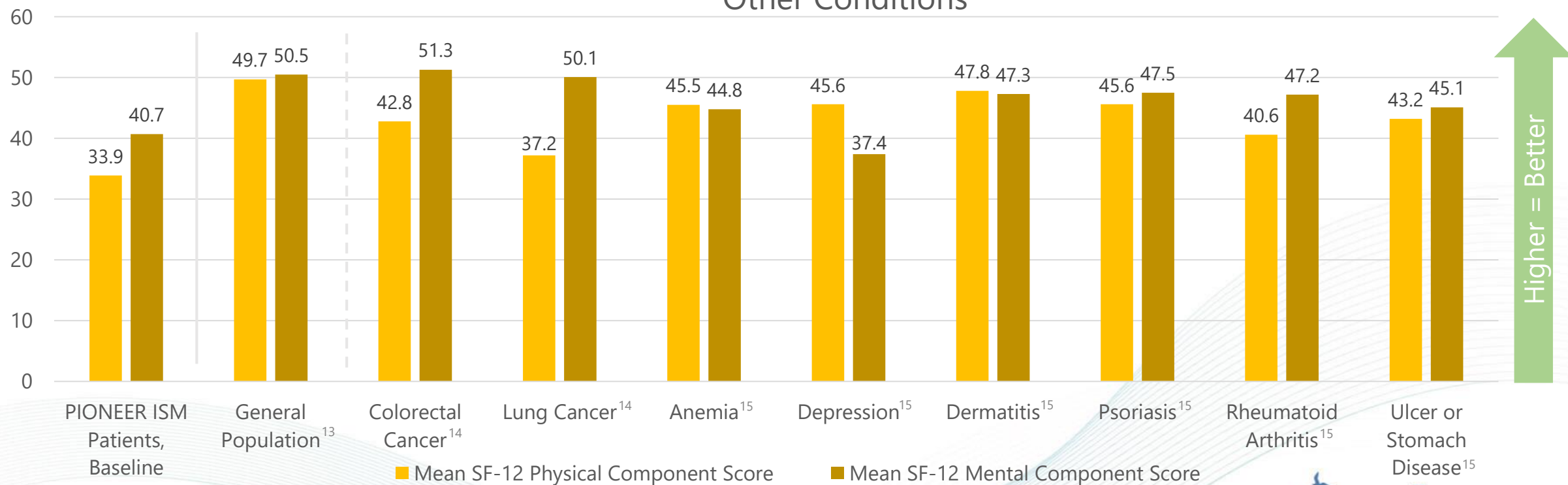
61.4%

Reported All 11 Symptoms

ISM-SAF: Indolent Systemic Mastocytosis Symptom Assessment Form

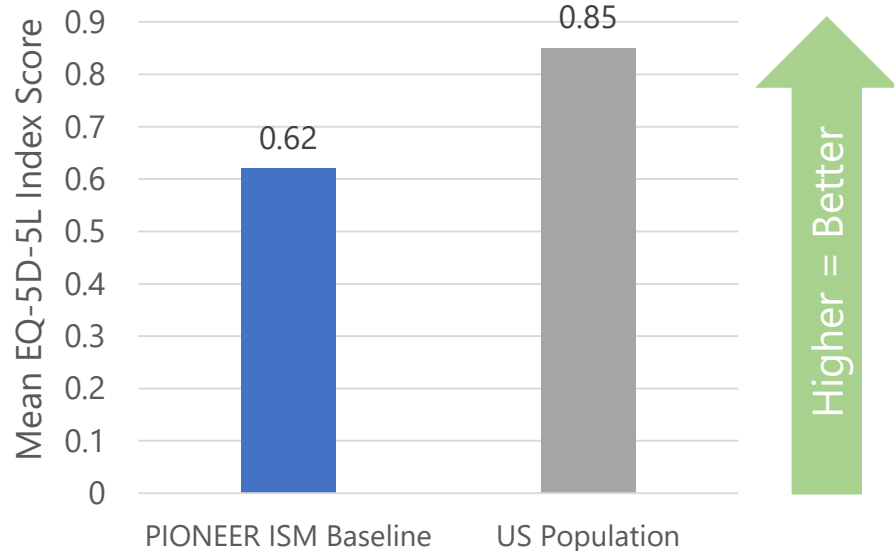
PIONEER Patients Reported Worse SF-12 Scores Compared to Patients With Other Chronic Conditions and Cancers

SF-12 Physical and Mental Component Scores from PIONEER, General Population, and Other Conditions



PIONEER Patients Reported EQ-5D-5L Index Scores Lower Than the US General Population and Rated Symptom Severity as Moderate to Very Severe on the PGIS

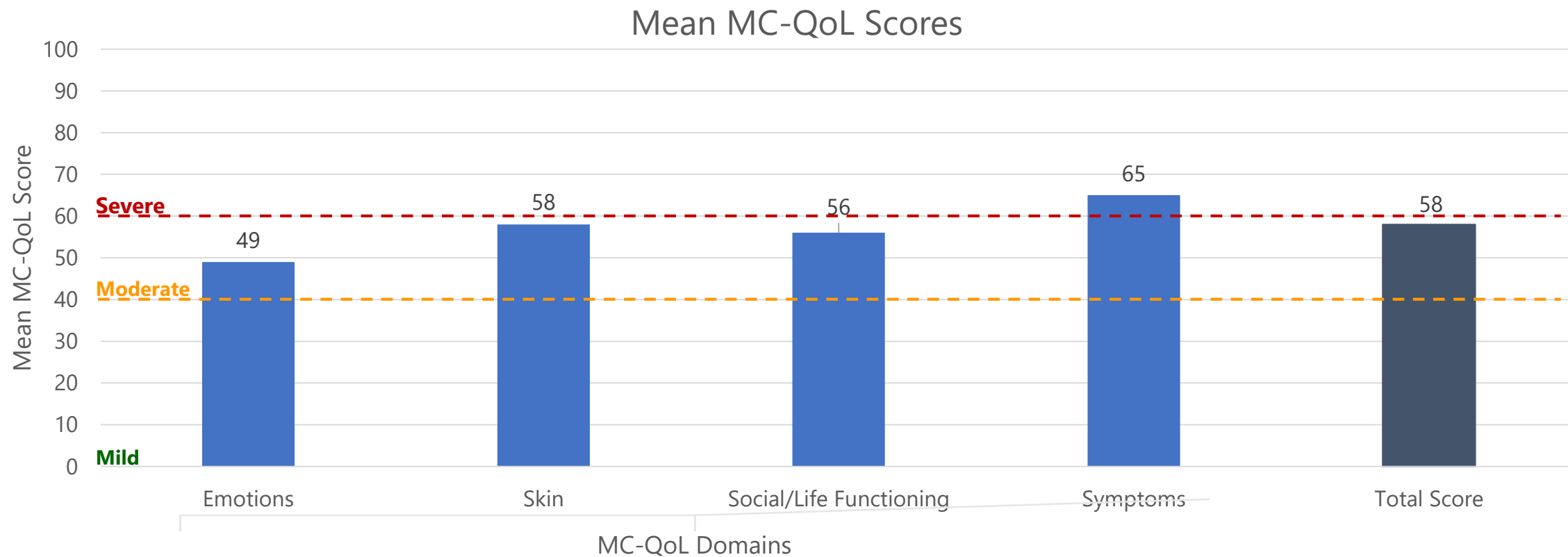
Mean EQ-5D-5L Scores, PIONEER ISM Patients and US Population



Patient Global Impression of Severity (PGIS)

- **92.2%** of patients rated their baseline symptom severity as *moderate* to *very severe*;
- **55.7%** rated their symptoms as *severe* or *very severe*.

PIONEER Patients Reported Moderate-to-severe Disease Severity On MC-QoL



PIONEER is the first randomized, double-blind, placebo-controlled trial of a highly selective KIT D816V-targeting agent in patients with Indolent SM.

Patients enrolled in PIONEER reported moderate-to-severe ISM symptoms despite best supportive care medicines.

Impaired health status, poor physical functioning and quality of life were shown in trial patients at baseline indicating high disease burden.

Acknowledgements

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