Detailed data from registrational PIONEER study demonstrate broad impact of AYVAKIT in patients with ISM

AAAAI 2023 Annual Meeting

February 27, 2023

Agenda

INTRODUCTION	**Kate Haviland,** Chief Executive Officer, Blueprint Medicines
PIONEER TRIAL RESULTS	**Mariana Castells, MD, PhD,** Director, Mastocytosis Center, Brigham and Women’s Hospital
DISCUSSION	**Becker Hewes, MD,** Chief Medical Officer, Blueprint Medicines
Q&A	

Forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans, strategies, timelines and expectations for Blueprint Medicines' current or future approved drugs and drug candidates, including approvals and launches, the initiation of clinical trials or the results of ongoing and planned clinical trial; Blueprint Medicines' plans, strategies and timelines to nominate development candidates; timelines and expectations for interactions with the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA) and other regulatory authorities; statements regarding the plans and potential benefits of AYVAKIT in treating patients with indolent SM; statements regarding plans and expectations for Blueprint Medicines' current or future approved drugs and drug candidates; the potential benefits of any of Blueprint Medicines' current or future approved drugs or drug candidates in treating patients; and Blueprint Medicines' financial performance, strategy, goals and anticipated milestones, business plans and focus. The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this presentation are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation: the risk that the partial clinical hold on the VELA trial may or may not be resolved in a timely manner; there may be additional adverse events observed that could impact the extent of the partial clinical hold or Blueprint Medicines' resolution of the partial clinical hold; there may be amendments to the trial protocol that impact the timing of the trial or evaluation of the data; preliminary activity and safety data may not be representative of more mature data; the COVID-19 pandemic may impact Blueprint Medicines' business, operations, strategy, goals and anticipated milestones, including ongoing and planned research and discovery activities, Blueprint Medicines' ability to conduct ongoing and planned clinical trials; the risk of delay of any current or planned clinical trials or the development of Blueprint Medicines' current or future drug candidates; risks related to Blueprint Medicines' ability to successfully demonstrate the safety and efficacy of its drug candidates and gain approval of its drug candidates on a timely basis, if at all; preclinical and clinical results for Blueprint Medicines' drug candidates may not support further development of such drug candidates either as monotherapies or in combination with other agents or may impact the anticipated timing of data or regulatory submissions; the timing of the initiation of clinical trials and trial cohorts at clinical trial sites and patient enrollment rates may be delayed or slower than anticipated; actions of regulatory agencies may affect the initiation, timing and progress of clinical trials; risks related to Blueprint Medicines' ability to obtain, maintain and enforce patent and other intellectual property protection for its products and current or future drug candidates it is developing; and the success of Blueprint Medicines' current and future collaborations, financing arrangements, partnerships or licensing arrangements. Any forward-looking statements contained in this press release represent Blueprint Medicines' views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Blueprint Medicines explicitly disclaims any obligation to update any forward-looking statements contained in this presentation as a result of new information, future events or otherwise. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements.

This presentation also contains estimates, projections and other statistical data made by independent parties and by Blueprint Medicines relating to market size and growth and other data about Blueprint Medicines' industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of Blueprint Medicines' future performance and the future performance of the markets in which the company operates are necessarily subject to a high degree of uncertainty and risk.

INTRODUCTION

KATE HAVILAND

CHIEF EXECUTIVE OFFICER
BLUEPRINT MEDICINES

AYVAKIT achieved the primary and all key secondary endpoints

PIONEER

		P VALUE[1]
Primary Endpoint	Mean Change in TSS	0.003
Secondary Endpoints	≥30% Reduction in TSS	0.009
	≥50% Reduction in TSS	0.005
	Mean Change in Most Severe Symptom Score[2]	0.015
	≥50% Reduction in Serum Tryptase	<0.0001
	≥50% Reduction in KIT D816V VAF	<0.0001
	≥50% Reduction in Bone Marrow MC Aggregates	<0.0001

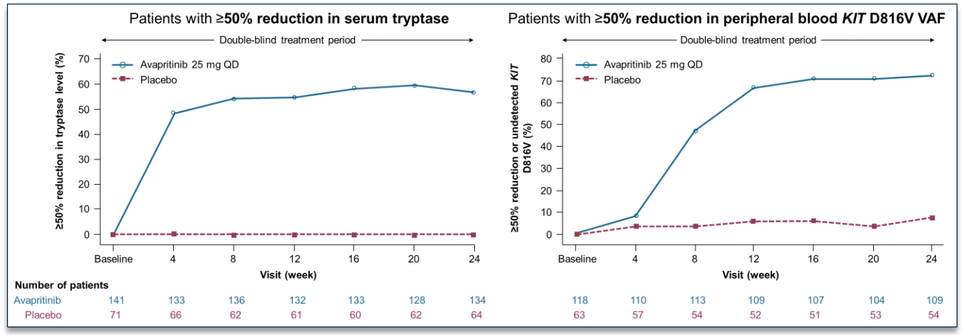
AYVAKIT was well-tolerated, with a safety profile favorable to placebo

TSS, total symptom score; VAF, variant allele fraction; MC, mast cell.

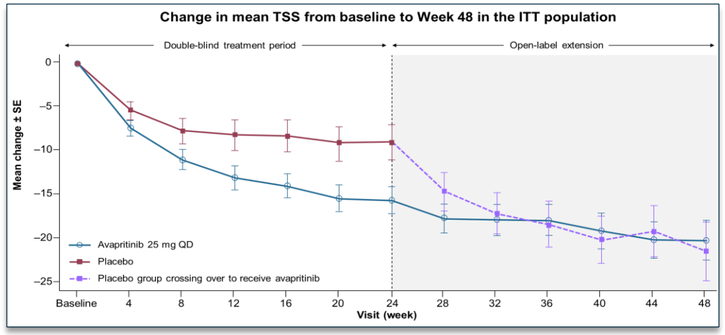
Clinically meaningful impact across diversity of measures

AYVAKIT®
avapritinib | tablets

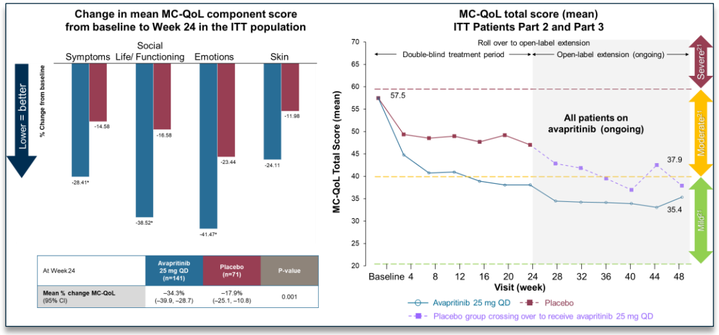
1 RAPID AND SUSTAINED DECREASES IN MAST CELL BURDEN



2 IMPROVED SYMPTOMS WITH DEEPENED RESPONSES OVER TIME



3 IMPROVED QUALITY-OF-LIFE



AYVAKIT showed systemic impact with a safety profile supportive of chronic treatment

1. Blueprint Medicines PIONEER data

Blueprint is the leader in SM, with AYVAKIT anchoring our franchise

ROBUST RESEARCH & DEVELOPMENT CAPABILITY

- >500 patient years of AYVAKIT clinical data in SM
- AYVAKIT granted FDA breakthrough therapy designations for advanced and moderate-to-severe ISM
- AYVAKIT/AYVAKYT is FDA and EMA approved for advanced SM

GLOBAL COMMERCIAL INFRASTRUCTURE

- $111M in global AYVAKIT net sales in 2022, representing 2x YoY growth
- ~500 U.S. patients on therapy
- ~400 U.S. accounts with experience
- Ongoing EU launch in advanced SM

MAST CELL DISORDER FRANCHISE STRATEGY

- AYVAKIT/AYVAKYT marketing applications for ISM under review in the U.S. and EU
- Ongoing Phase 2/3 HARBOR trial of elenestinib in patients with ISM
- Wild-type KIT research program for chronic spontaneous urticaria

Blueprint 2027: Doubling our impact, in half the time

blueprint™ 2027

	2011-2022	Planned 2022-2027
Approved medicines	2	4+
Disease leadership areas	1	3+
Late-stage clinical programs	2	4+
Research platforms	1	2
Cumulative development candidates	14	25+

PIONEER RESULTS

DR. MARIANA CASTELLS, MD, PHD

DIRECTOR, MASTOCYTOSIS CENTER

BRIGHAM AND WOMEN'S HOSPITAL

blueprint™ MEDICINES

Dr. Mariana Castells, MD, PhD

- Brigham and Women’s Hospital, Boston
  - Director, Mastocytosis Center
  - Director, Drug Hypersensitivity and Desensitization Center
- Professor, Harvard Medical School
- Board of Directors: AAAAI, ABAI
  - AAAAI Foundation Research Chair
- PIONEER trial investigator

AAAAI, American Academy of Allergy, Asthma & Immunology; ABAI, American Board of Allergy and Immunology.

Efficacy and Safety of Avapritinib in Indolent Systemic Mastocytosis (ISM): Results from the Double-Blind Placebo-Controlled PIONEER Study

Mariana Castells,[1*] Jason Gotlib,[2*] Hanneke Oude Elberink,[3] Frank Siebenhaar,[4,5] Karin Hartmann,[6,7] Sigurd Broesby-Olsen,[8] Tracy I. George,[9] Jens Panse,[10] Ivan Alvarez-Twose,[11] Deepti H. Radia,[12] Tsewang Tashi,[13] Cristina Bulai Livideanu,[14] Vito Sabato,[15] Paul Van Daele,[16] Sonia Cerquozzi,[17] Ingunn Dybedal,[18] Andreas Reiter,[19] Thanai Pongdee,[20] Stéphane Barete,[21] Lawrence Schwartz,[22] Prithviraj Bose,[23] Massimo Triggiani,[24] William Shomali,[2] Matthew Giannetti,[25] Ilda Bidollari,[26] Hui-Min Lin,[26] Robyn Scherber,[26] Maria Roche,[26] Cem Akin,[27] Marcus Maurer[4,5**]**

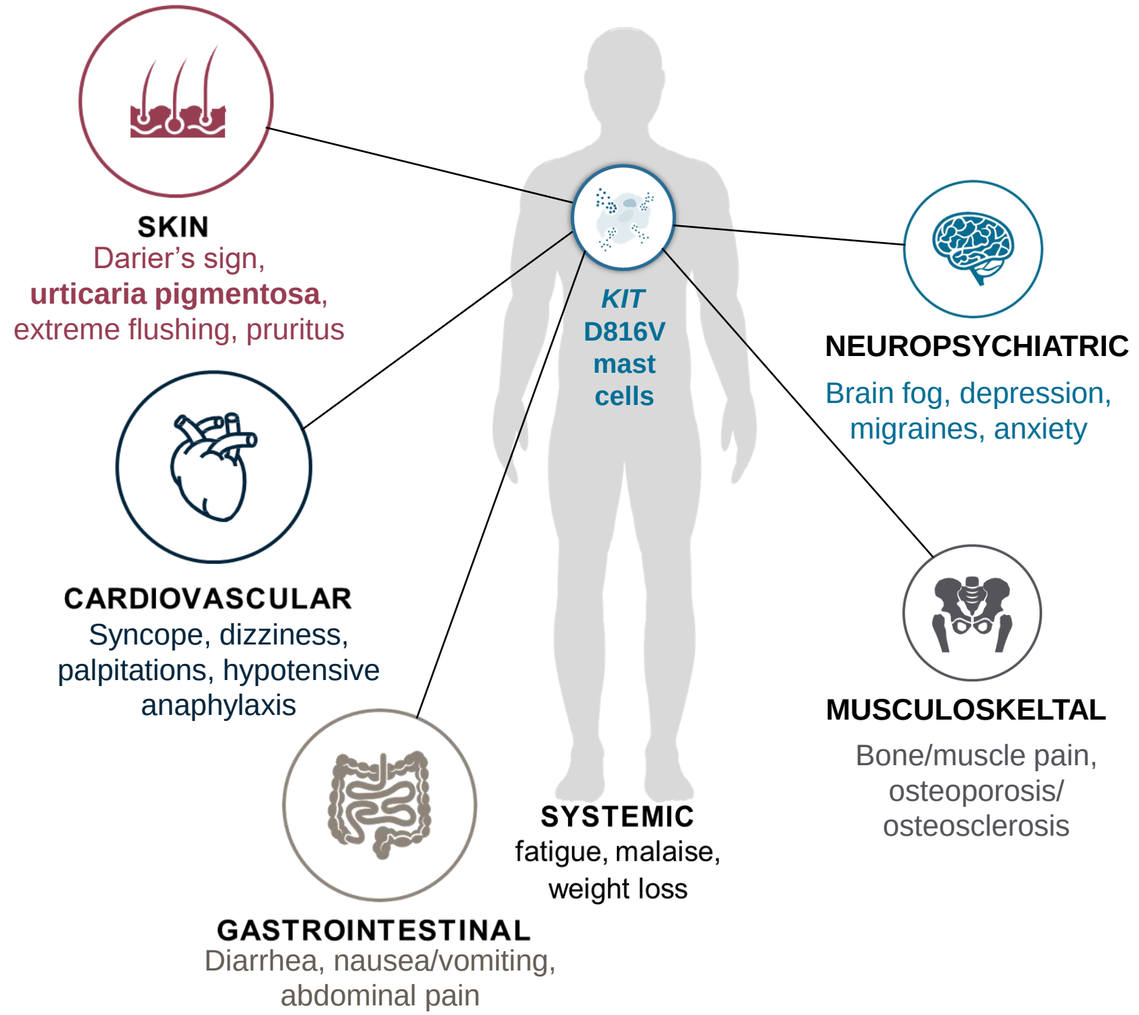
***Equally contributing first authors; **Equally contributing last authors**

[1]Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA; [2]Stanford Cancer Institute / Stanford University School of Medicine, Stanford, CA, USA; [3]Department of Allergology, University Medical Center Groningen, University of Groningen, Groningen, Netherlands; [4]Institute of Allergology, Charité – Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany; [5]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Allergology and Immunology, Berlin, Germany; [6]Division of Allergy, Department of Dermatology, University Hospital Basel and University of Basel, Basel, Switzerland; [7]Department of Biomedicine, University Hospital Basel and University of Basel, Basel, Switzerland; [8]Department of Dermatology and Allergy Centre, Odense University Hospital, Odense, Denmark; [9]ARUP Laboratories, Department of Pathology, University of Utah School of Medicine, Salt Lake City, UT, USA; [10]Department of Oncology, Hematology, Hemostaseology and Stem Cell Transplantation, University Hospital Aachen, Medical Faculty, RWTH Aachen University, Aachen, Germany; [11]Institute of Mastocytosis Studies of Castilla-La Mancha, Toledo, Spain; [12]Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom; [13]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [14]Département de dermatologie, CEREMAST CHU de Toulouse, Toulouse, France; [15]Department of Immunology, Allergology and Rheumatology, University of Antwerp and Antwerp University Hospital, Antwerp, Belgium; [16]Department of Internal Medicine, Erasmus Medical Center, Rotterdam, Netherlands; [17]Department of Medicine, Alberta Health Services and Cumming School of Medicine, University of Calgary, Calgary, AB, Canada; [18]Department of Hematology, Oslo University Hospital, Oslo, Norway; [19]University Hospital Mannheim, Heidelberg University, Mannheim, Germany; [20]Division of Allergic Diseases, Mayo Clinic, Rochester, MN, USA; [21]Unit of Dermatology Reference Centre for Mastocytosis (CEREMAST) AP-HP, Pitié-Salpêtrière Hospital, Sorbonne Université, Paris, France; [22]Department of Internal Medicine, Virginia Commonwealth University, Richmond, VA, USA; [23]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [24]Division of Allergy and Clinical Immunology, University of Salerno, Salerno, Italy; [25]Division of Allergy and Clinical Immunology, Brigham and Women's Hospital, Boston, MA, USA; [26]Blueprint Medicines Corporation, Cambridge, MA, USA; [27]University of Michigan, Ann Arbor, MI, USA.

AAAAI Annual Meeting, San Antonio, TX; February 24–27, 2023

Indolent systemic mastocytosis (ISM) is a clonal mast cell disease driven by the KIT D816V mutation in ~ 95% of adult cases[1–3]

- Patients with **ISM** can have lifelong **debilitating symptoms** across multiple organ systems[4–8]
- Most patients rely on polypharmacy for the management of symptoms with best supportive care **(BSC) medications**[8–10]
- Symptoms are **not adequately controlled** with BSC medications in many patients with ISM[8–10]
- Currently, there are **no approved therapies** that target the **KIT D816V-mutated** tyrosine kinase in ISM



BSC, best supportive care; ISM, indolent systemic mastocytosis.

Avapritinib is a potent and highly selective oral therapy targeting KIT D816V, the underlying driver of systemic mastocytosis

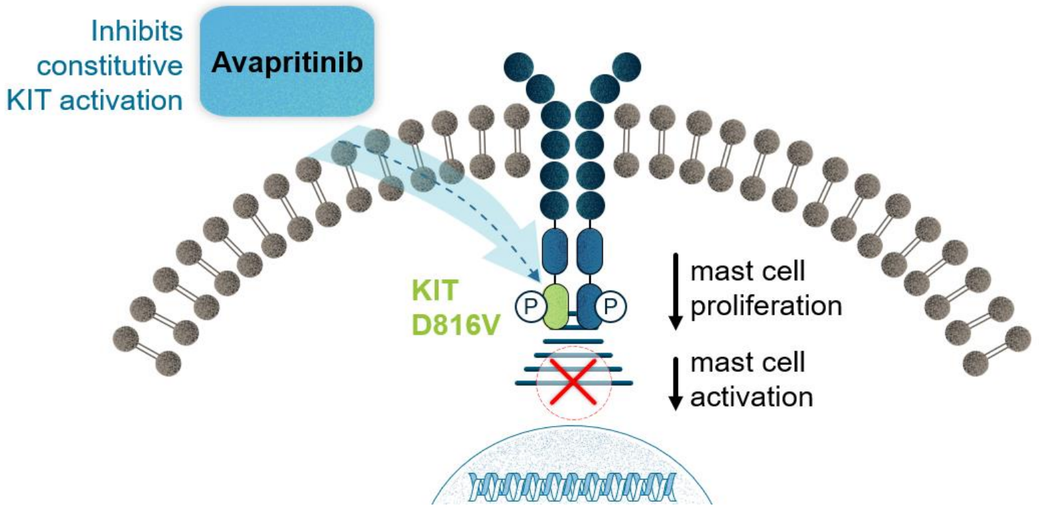
Highly selective kinome profile

Potently and selectively inhibits the autophosphorylation of KIT D816V, with an IC_{50} of 0.27 nanomolar in selective cellular assays[11]

Biochemical IC_{50} (nM)

	KIT D816V	KIT wild type
Avapritinib	0.27	73

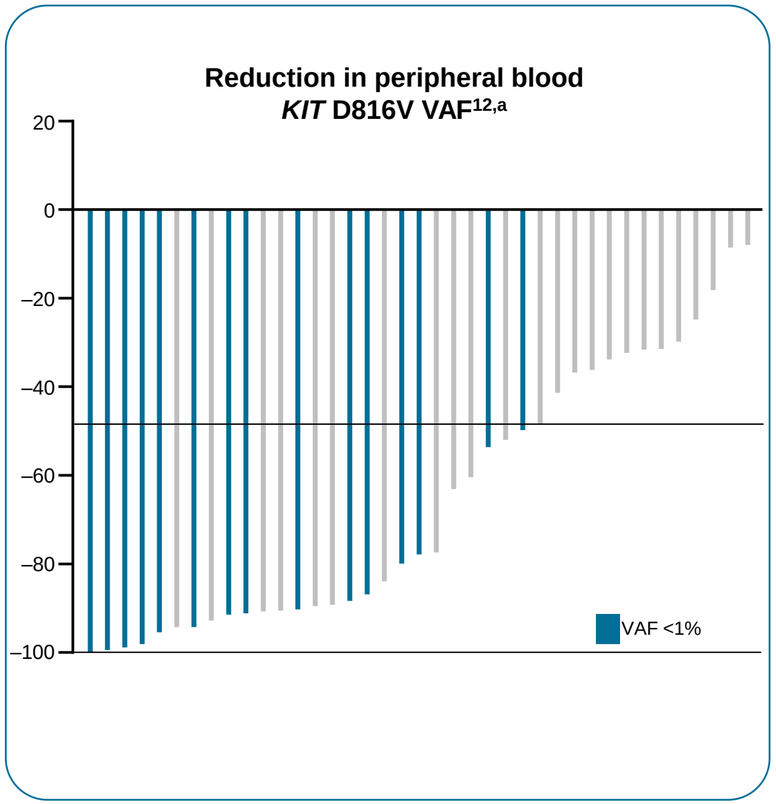
Avapritinib kinase inhibitor activity



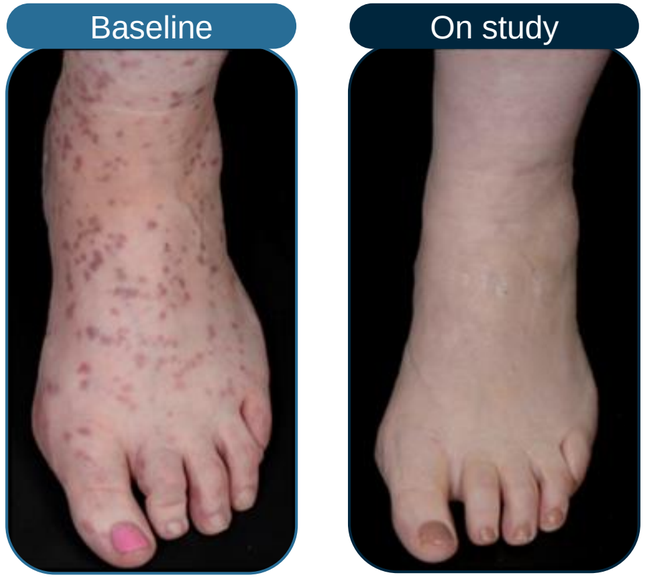
nM, nanomolar concentration.

Avapritinib in advanced systemic mastocytosis

Reduction in mast cell burden biomarkers[12,13]



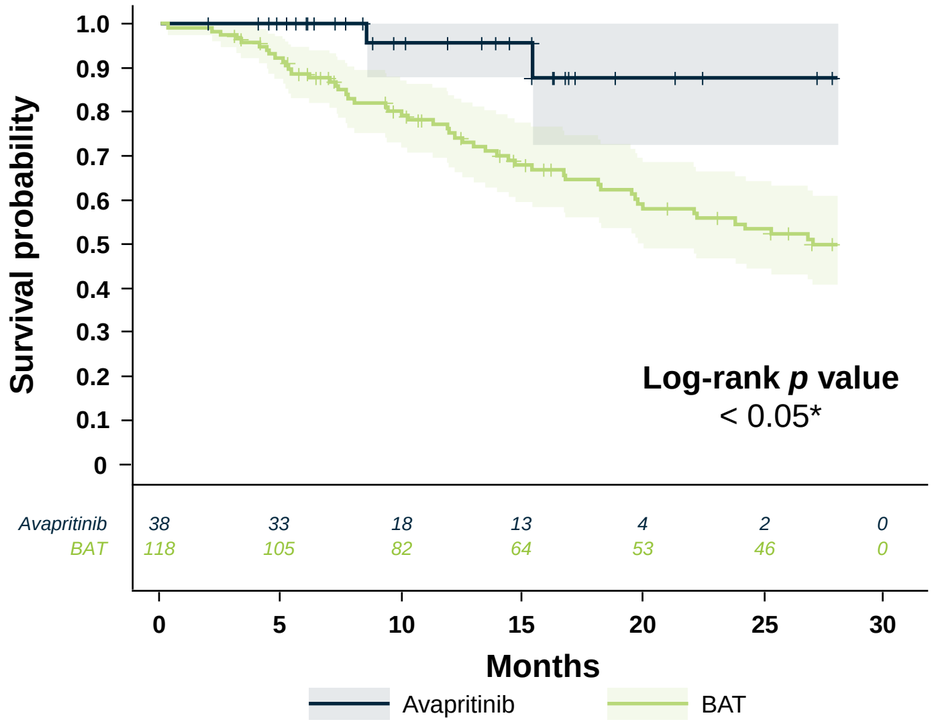
Improved symptom severity[12,13]



Patient permission granted for use of photos

Patients experienced an improvement in all AdvSM symptoms per the AdvSM-SAF[12,13]

Survival benefit vs. real-world best available therapy[14,b]



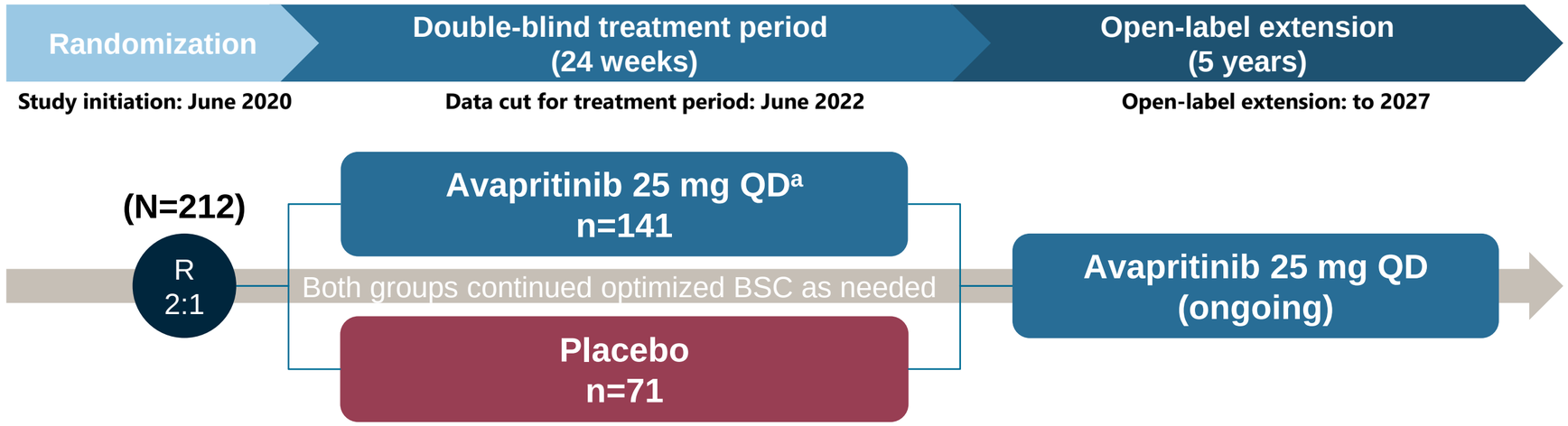
Avapritinib is approved in the US and EU for AdvSM with a starting dose of 200 mg once daily[15,16]

[a]Patients with systemic mastocytosis and an associated hematologic neoplasm only. [b]Data for best available therapy from retrospective real-world patient chart review, methodology described previously; shading represents 95% confidence interval.[17] AdvSM, advanced systemic mastocytosis. AdvSM-SAF, advanced systemic mastocytosis symptom assessment form.

Registrational PIONEER study: Randomized, double-blind, placebo-controlled study in patients with ISM

Screening period

- Best supportive care medications (BSC) optimized for up to a month
  - Antihistamines, cromolyn, anti-IgE antibody, leukotriene receptor antagonists, corticosteroids, etc.
- Eligibility
  - Age ≥18 years
  - ISM by central pathology review
  - Moderate to severe symptoms (TSS ≥28) after ≥2 BSC medications



Symptoms
Primary endpoint

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

- Mean change in **individual symptom scores** of ISM-SAF
- Mean change in **most severe symptom score**

Biomarkers of mast cell burden
Key secondary endpoints

- ≥50% reduction in **serum tryptase** levels
- ≥50% reduction in ***KIT* D816V VAF** in peripheral blood (or below level of detection [<0.02%] for patients with a detectable mutation at baseline)
- ≥50% reduction in in bone marrow **mast cell aggregates**

Quality of life

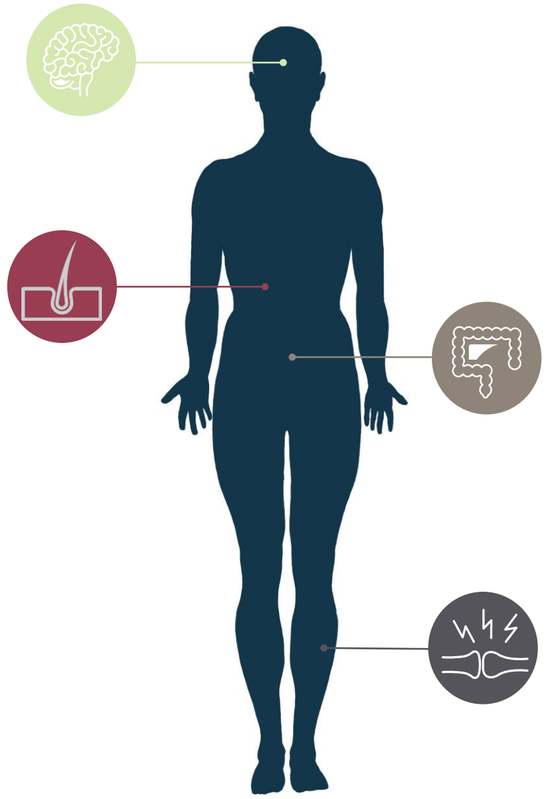
- Mean % change in QoL score, as measured by **MC-QoL**

[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). Patients treated with high dose steroids within 7 days of primary endpoint (n=4) were excluded from the week 24 analysis, but included at other timepoints of the study. Percentages were calculated based on available data at the timepoint. One-sided P-values are reported for primary and key secondary endpoints. ISM-SAF, Indolent Systemic Mastocytosis-Symptom Assessment Form; MC-QoL, Mastocytosis Quality of Life Questionnaire; QD, once daily; QoL, quality of life; R, randomized; TSS, total symptom score; VAF, variant allele fraction.

ISM-SAF: Validated symptom assessment tool specifically developed for evaluation of ISM symptomology[18–20]

ISM-SAF

- Total Symptom Score (TSS) based on severity of 11 ISM symptoms
- Developed over past 8 years with input from patients, disease experts, and global regulatory agencies[19]



ISM Symptom Assessment Form (ISM-SAF)	
ISM Symptom	**Scoring**
Abdominal pain Diarrhea Nausea	Scored 0–10 daily on handheld device 0 = no symptom 10 = **worst imaginable** symptom Analyzed as a 14-day moving average
Spots Itching Flushing	
Brain Fog Headache Dizziness	
Bone pain Fatigue	

TSS (0–110)
Higher scores represent more severe symptoms

Baseline patient and disease characteristics were balanced between groups

Patient demographic	Avapritinib 25 mg QD (n=141)	Placebo (n=71)
Age (years), median (range)	50.0 (18–77)	54.0 (26–79)
Female, n (%)	100 (70.9)	54 (76.1)
ISM symptom burden		
TSS score, mean (SD)	50.2 (19.1)	52.4 (19.8)
Most severe symptom score, mean (SD)	7.7 (1.7)	7.9 (1.7)
Mast cell burden		
Median serum tryptase (central), ng/mL (range)	38.4 (3.6–256.0)	43.7 (5.7–501.6)
Median bone marrow biopsy mast-cells (central), % (range)	7.0 (1.0–50.0)	7.0 (1.0–70.0)
Mast-cell aggregates present, n (%)	106 (75.2)	57 (80.3)
Median *KIT* D816V VAF in peripheral blood, % (range)[a]	0.4 (0.02–41.3)	0.3 (0.02–36.7)
KIT D816V positivity, n (%)	131 (92.9)	69 (97.2)

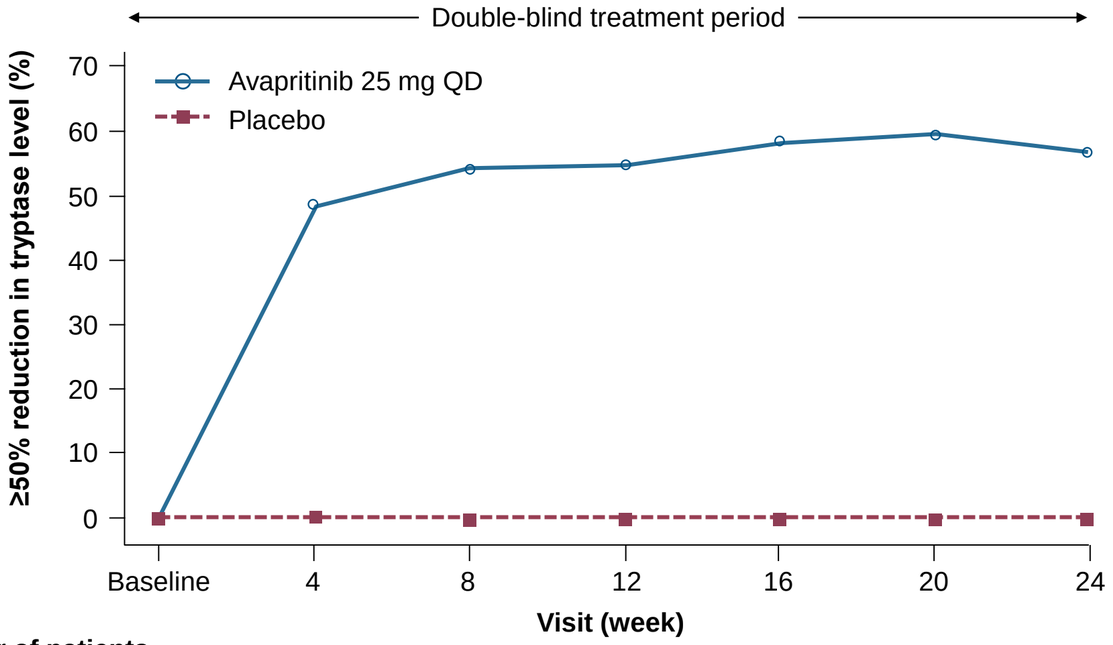
SM therapy	Avapritinib 25 mg QD (n=141)	Placebo (n=71)
Prior cytoreductive therapy, n (%)[b]	19 (13.5)	7 (9.9)
Prior TKI therapy, n (%)	10 (7.1)	4 (5.6)
BSC use		
Number of BSC treatments, median (range)	3 (0-11)	4 (1-8)
BSC use at baseline, n (%)[c]	140 (99.3)	71 (100.0)
H1 Antihistamines	137 (97.2)	71 (100.0)
H2 Antihistamines	93 (66.0)	47 (66.2)
Leukotriene receptor antagonists	49 (34.8)	25 (35.2)
Cromolyn sodium	43 (30.5)	25 (35.2)
Proton pump inhibitors	22 (15.6)	20 (28.2)
Corticosteroids	17 (12.1)	7 (9.9)
Anti-IgE antibody (omalizumab)	14 (9.9)	7 (9.9)
Other	33 (23.4)	19 (26.8)

[a]The limit of detection was 0.02%. [b]Cytoreductive therapies included dasatinib, imatinib, masitinib, nilotinib, midostaurin, brentuximab vedotin, cladribine, hydroxyurea, rapamycin, and interferon alfa. Includes treatments received by patients at baseline; patients may have received BSC treatments previously that had been discontinued at the time of enrollment/baseline.
[c]All patients had at least two BSC prior to or at screening. A total of 10 (7.1%) patients treated with avapritinib and 5 (7.0%) patients treated with placebo had <2 BSC at the start of the study.
ISM, indolent systemic mastocytosis; SD, standard deviation; SM, systemic mastocytosis; TKI, tyrosine kinase inhibitor; TSS, total symptom score.

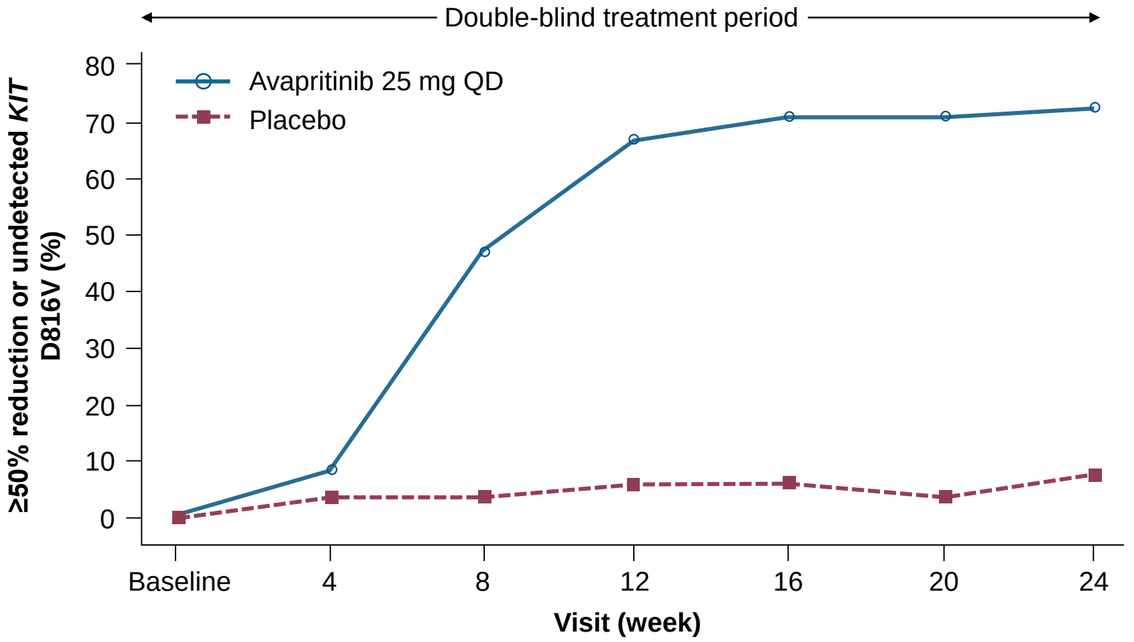
Rapid and sustained reductions in biomarkers of mast cell burden in avapritinib-treated patients *versus* placebo

Key secondary endpoints

Patients with ≥**50% reduction in serum tryptase**



Patients with ≥**50% reduction in peripheral blood *KIT* D816V VAF**



Number of patients

Avapritinib	141	133	136	132	133	128	134	118	110	113	109	107	104	109
Placebo	71	66	62	61	60	62	64	63	57	54	52	51	53	54

At Week 24	Avapritinib 25 mg QD (n=141)	Placebo (n=71)	P-value
Proportion of patients with **≥50% reduction in serum tryptase** (95% CI)	53.9% (45.3–62.3)	0.0% (0.0–5.1)	<0.0001

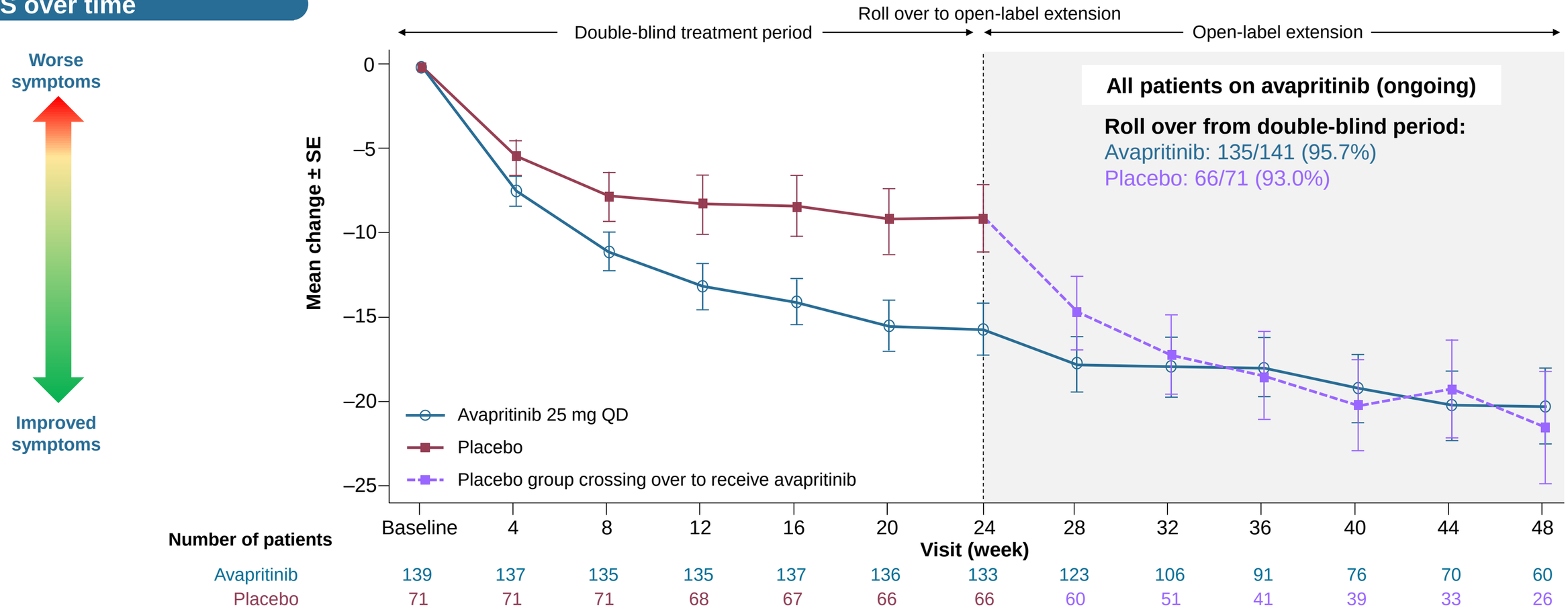
At Week 24	Avapritinib 25 mg QD (n=141)	Placebo (n=71)	P-value
Proportion of patients with **≥50% reduction in *KIT* D816V VAF** (95% CI)	67.8% (58.6–76.1)	6.3% (1.8–15.5)	<0.0001

At Week 24	Avapritinib 25 mg QD (n=141)	Placebo (n=71)	P-value
Proportion of patients with **≥50% reduction in BM mast cell aggregates** (95% CI)	52.8% (42.9–62.6)	22.8% (12.7–35.8)	<0.0001

BM, bone marrow; CI, confidence interval.

Avapritinib demonstrated significant and durable improvement in symptoms *versus* placebo

TSS over time



Number of patients	Baseline	4	8	12	16	20	24	28	32	36	40	44	48
Avapritinib	139	137	135	135	137	136	133	123	106	91	76	70	60
Placebo	71	71	71	68	67	66	66	60	51	41	39	33	26

Primary endpoint

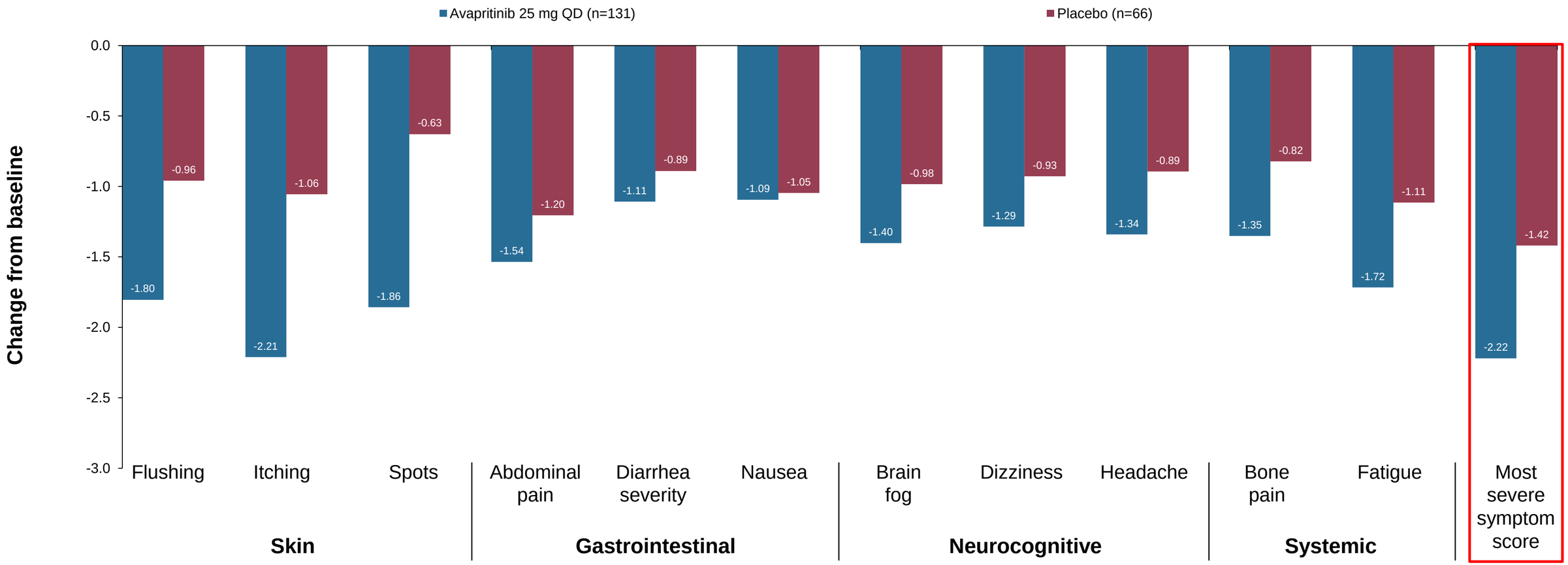
A one-sided P-value of <0.025 was needed to declare avapritinib as superior in reducing TSS versus placebo.

At Week 24	Avapritinib 25 mg QD (n=141)	Placebo (n=71)	P-value
Mean change in TSS (95% CI)	–15.58 (–18.61, –12.55)	–9.15 (–13.12, –5.18)	0.003

SE, standard error of the mean.

Avapritinib demonstrated improvement in all individual ISM symptoms *versus* placebo including the most severe symptom at baseline

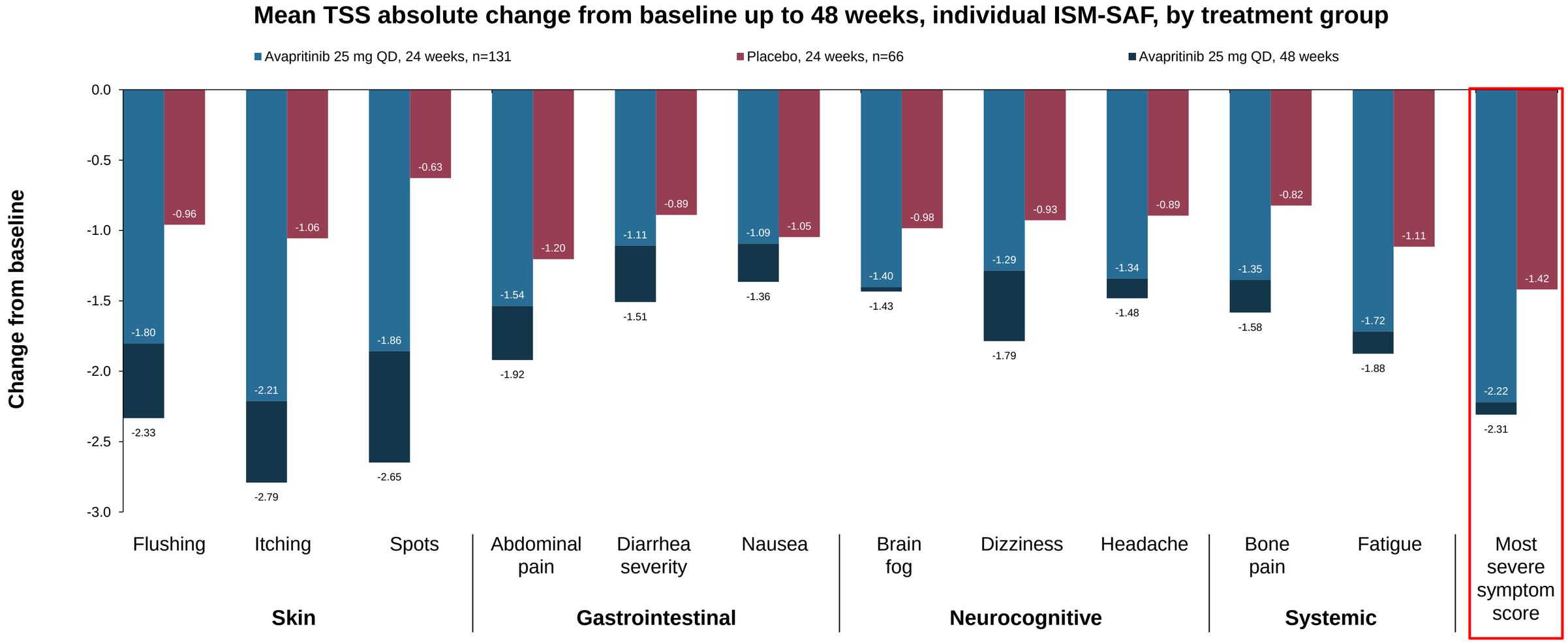
Mean TSS absolute change from baseline to 24 weeks, individual ISM-SAF, by treatment group



At Week 24	Avapritinib 25 mg QD (n=131)	Placebo (n=66)	P-value
Mean change in most severe symptom score (SD)	–2.22 (2.30)	–1.42 (1.88)	0.015

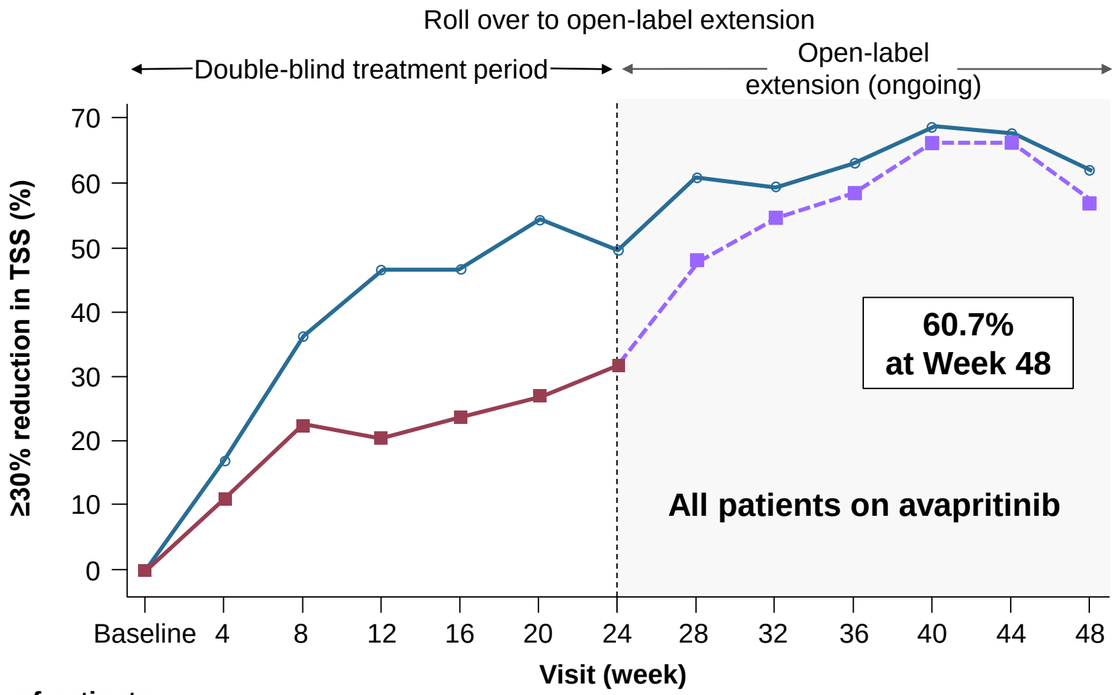
Regardless of which symptom was rated most severe at baseline, avapritinib patients had a significant reduction in this versus placebo

Continued improvement was observed in all individual symptoms among avapritinib-treated patients at 48 weeks



Avapritinib-treated patients were significantly more likely than placebo to reach the TSS ≥30% and TSS ≥50% reduction thresholds over time

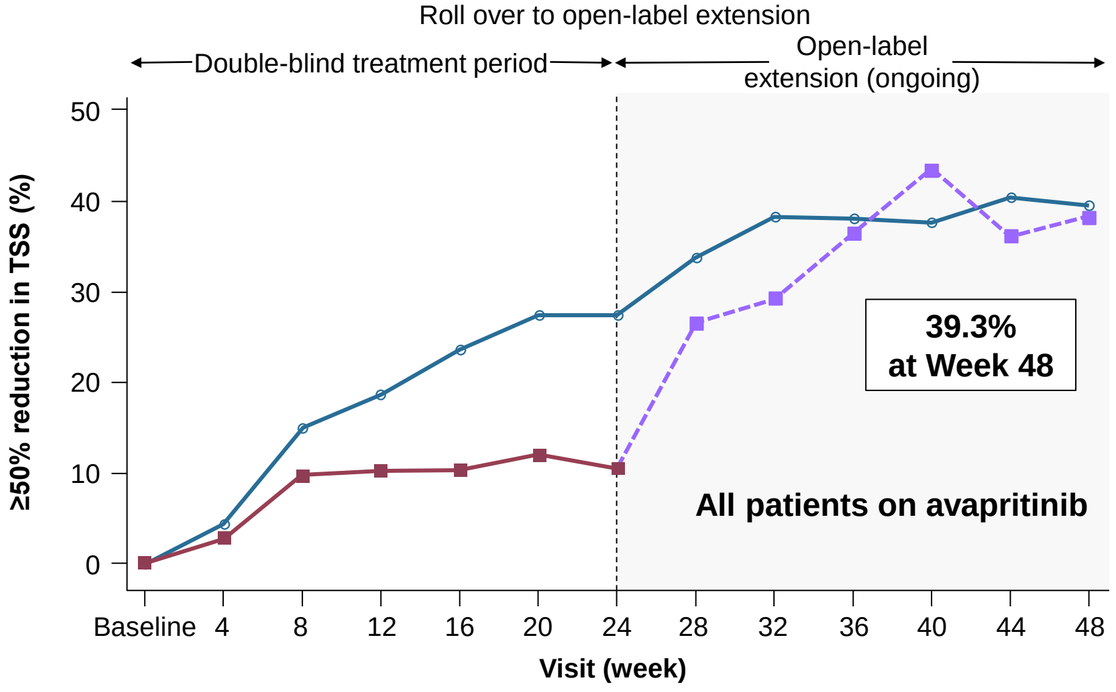
≥30% reduction in ISM-SAF TSS score over time



Number of patients

Avapritinib	139	135	133	133	135	134	131	121	104	89	74	69	58
Placebo	71	71	71	68	67	66	66	60	51	41	39	33	26

≥50% reduction in ISM-SAF TSS score over time



	139	135	133	133	135	134	131	121	104	89	74	69	58
	71	71	71	68	67	66	66	60	51	41	39	33	26

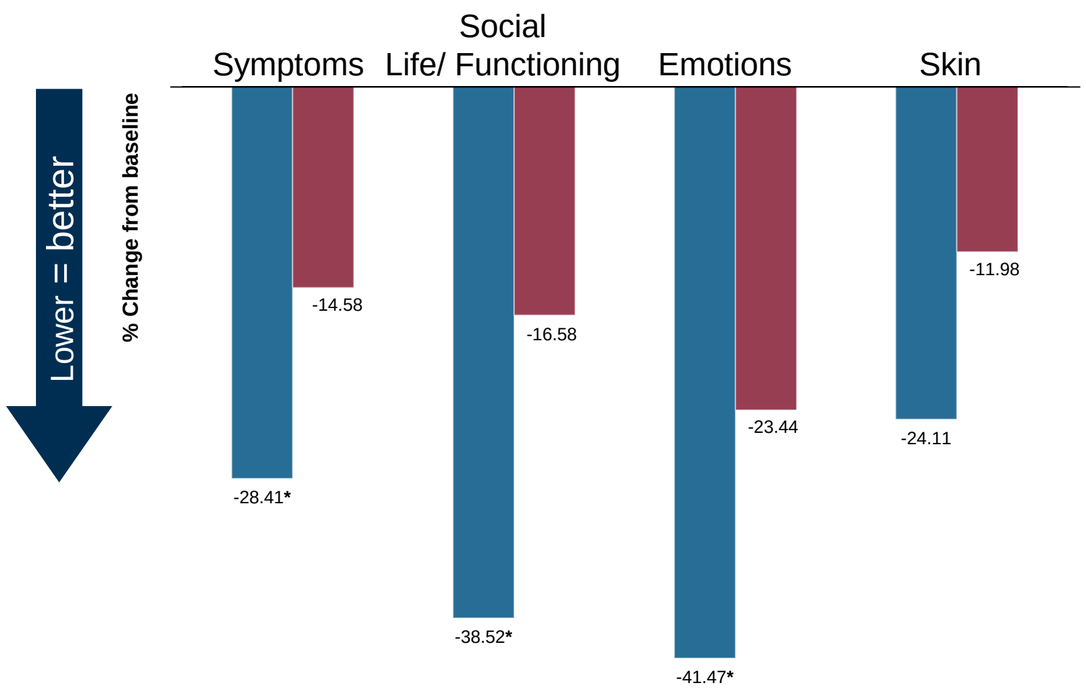
Treatment group: Avapritinib 25 mg QD; Placebo; Placebo group crossing over to receive avapritinib 25 mg QD

At Week 24	Avapritinib 25 mg QD (n=141)	Placebo (n=71)	P-value
Proportion of patients with **≥30% reduction in TSS** (95% CI)	45.4% (37.0–54.0)	29.6% (19.3–41.6)	0.009

At Week 24	Avapritinib 25 mg QD (n=141)	Placebo (n=71)	P-value
Proportion of patients with **≥50% reduction in TSS** (95% CI)	24.8% (17.9–32.8)	9.9% (4.1–19.3)	0.005

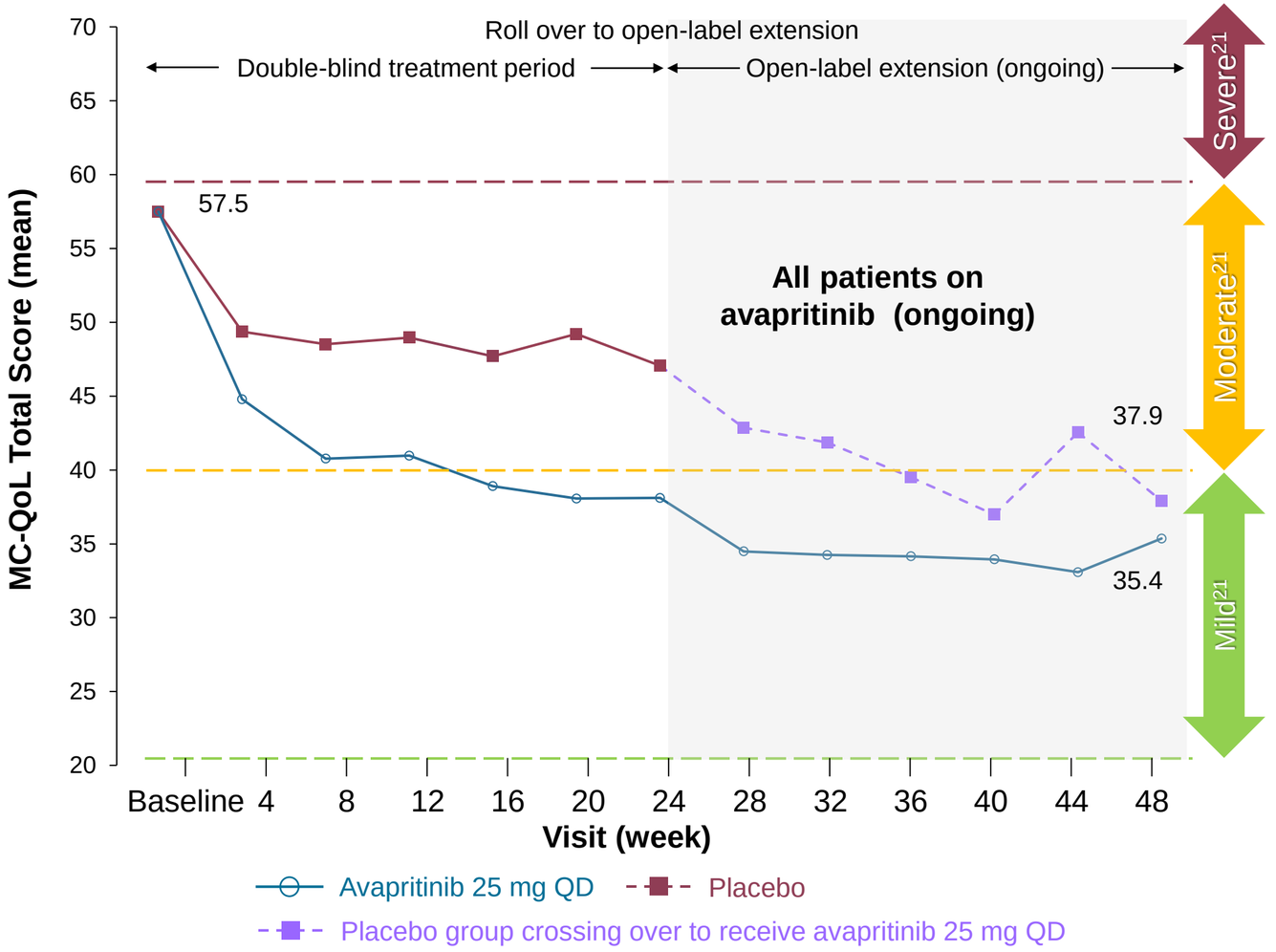
Avapritinib demonstrated sustained improvement in MC-QoL *versus* placebo, an established and validated disease-specific QoL measure

Change in mean MC-QoL component score from baseline to Week 24 in the ITT population



At Week 24	Avapritinib 25 mg QD (n=141)	Placebo (n=71)	P-value
Mean % change MC-QoL (95% CI)	–34.3% (–39.9, –28.7)	–17.9% (–25.1, –10.8)	0.001

MC-QoL total score (mean) ITT Patients Part 2 and Part 3



ITT, intent-to-treat. *p≤0.05.

Avapritinib 25mg QD was well tolerated, with a similar safety profile to placebo

- Majority of AEs were Grade 1 or 2 with a low rate of discontinuation
- SAEs were reported more frequently in the placebo group (no treatment-related SAEs in either group)
- Edema adverse events were higher in the avapritinib group (majority Grade 1, and did not result in discontinuation)

	Avapritinib 25 mg QD (N=141)	Placebo (N=71)
Any AEs[a,b], n (%)	128 (90.8)	66 (93.0)
Grade 1–2 AEs	98 (69.5)	51 (71.8)
Grade 1–2 related AEs	74 (52.5)	30 (42.3)
Grade ≥3 AEs	30 (21.3)	15 (21.1)
Grade ≥3 related AEs	3 (2.1)	2 (2.8)
SAEs, n (%)	7 (5.0)	8 (11.3)
Any grade TRAEs	77 (54.6)	32 (45.1)
Most frequently reported TRAEs (≥5% of patients)		
Headache	11 (7.8)	7 (9.9)
Nausea	9 (6.4)	6 (8.5)
Peripheral edema	9 (6.4)	1 (1.4)
Periorbital edema	9 (6.4)	2 (2.8)
Dizziness	4 (2.8)	5 (7.0)
TRAEs leading to discontinuation	2 (1.4)	1 (1.4)

[a]AEs refer to treatment-emergent AEs (TEAEs), defined as any AE that occurred between day 1 of Part 2 through to a day prior to day 1 of Part 3 if the patient crossed over to Part 3; if the patient did not cross over, then through 30 days after the last dose of study drug.
[b]There were too few events (≤5 per group) to assess the impact of avapritinib on anaphylaxis.
AEs, adverse events; SAEs, serious adverse events; TRAEs, treatment-related adverse events.

Summary

- ISM patients can suffer from a wide range of debilitating symptoms often not adequately controlled by BSC medications
- PIONEER is the first randomized, double-blind, placebo-controlled trial of a highly selective KIT D816V-targeting agent in patients with Indolent SM
- Avapritinib-treated patients showed rapid, durable and clinically meaningful improvements in mast cell burden, symptoms, and QoL compared to placebo-treated patients at 24 weeks of treatment
- Avapritinib was well tolerated with a similar safety profile to placebo
- Open-label extension assessing long-term safety and efficacy of 25 mg QD avapritinib ongoing

Conclusion

- Avapritinib selectively targets KIT D816V, the underlying driver of disease
- Avapritinib reduced mast cell burden, improved symptoms, and improved quality of life for patients, potentially offering a promising new treatment option for patients with ISM

Acknowledgements

- We thank the patients and their families for making this trial possible
- We also thank the investigators and clinical trial teams who participated in the trial
- Medical writing support was provided by Will Wheddon, MSci, and editorial support was provided by Travis Taylor, BA, all of Paragon, Knutsford, UK, supported by Blueprint Medicines Corporation, Cambridge, MA, according to Good Publication Practice guidelines

DISCUSSION

BECKER HEWES, MD

CHIEF MEDICAL OFFICER
BLUEPRINT MEDICINES

PIONEER trial population is representative of the real world

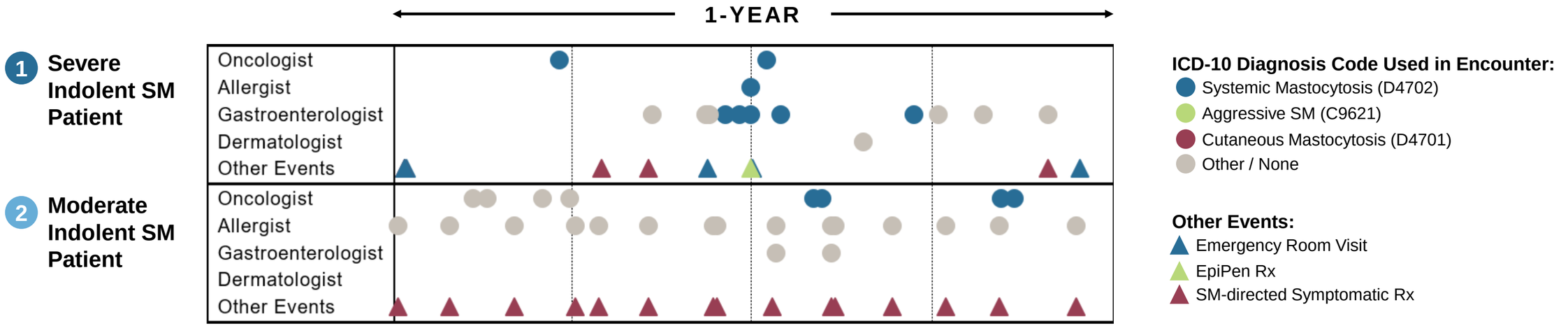
PIONEER TRIAL: AYVAKIT ARM BASELINE CHARACTERISTICS

3 Symptom-directed treatments (median)

50.2 points — Mean TSS (Possible range: 0-110)

57.5 points — Mean MC-QoL score (Possible range: 0-100)

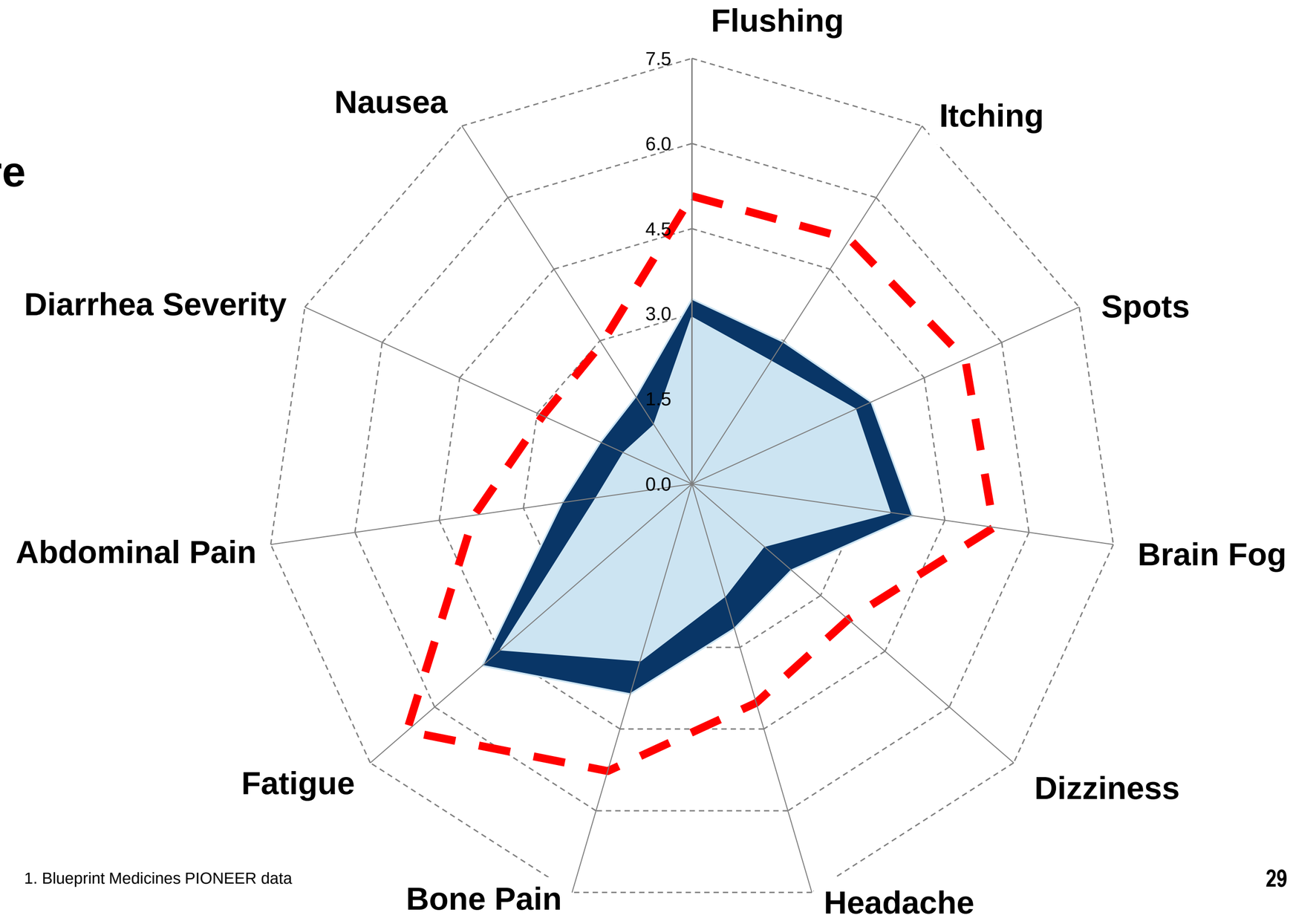
PATIENT JOURNEY VISIBLE IN U.S. CLAIMS DATA



1. Claims algorithm considers number & type of SM diagnosis codes, comorbidities including associated hematologic neoplasms (AHNs) and evidence of organ damage (e.g., splenomegaly, hepatomegaly, compromised bone, etc.), in addition to prescription therapies (e.g., trial of TKIs / cytoreductive therapies, cromolyn sodium, long-term steroid use, omalizumab, epi-pen, etc.). CM, cutaneous mastocytosis; ISM, indolent systemic mastocytosis. Both medical and pharmacy claims are captured.

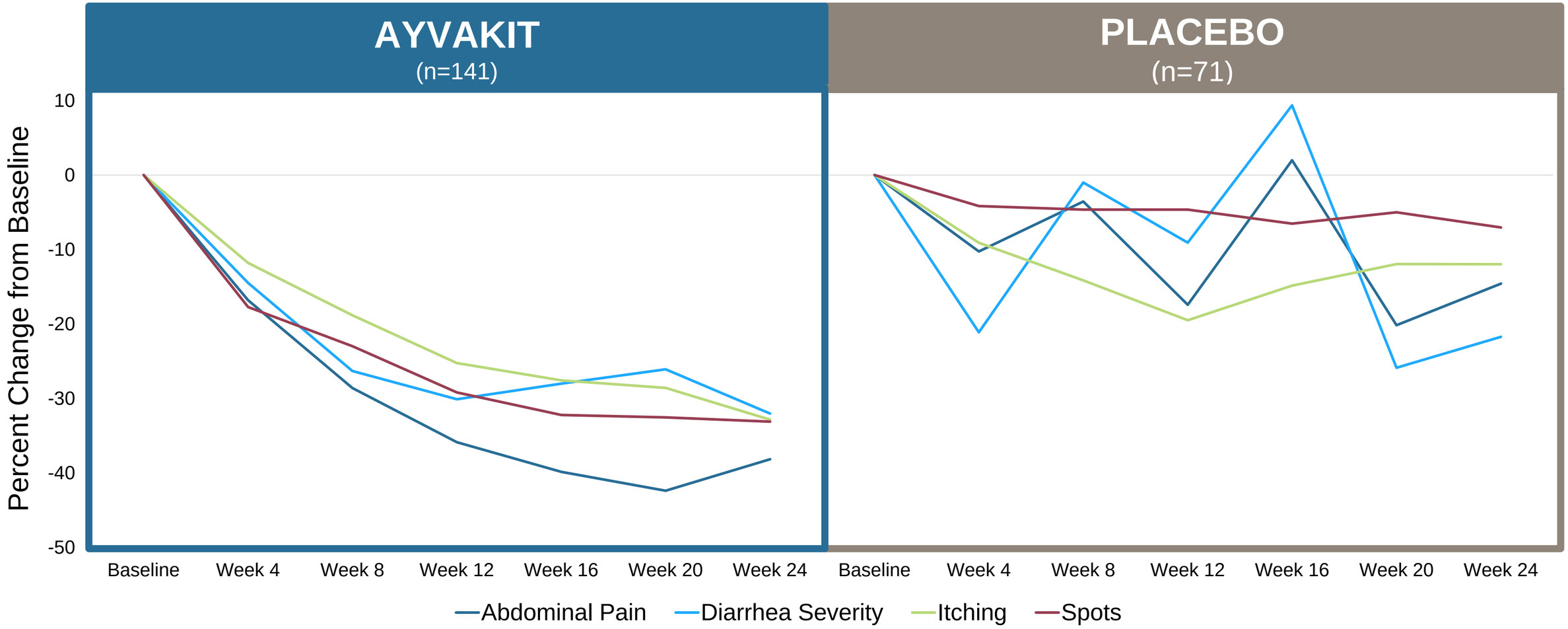
AYVAKIT showed consistent impact on all symptoms measured by the ISM-SAF

Mean absolute value of individual symptom score for AYVAKIT patients



1. Blueprint Medicines PIONEER data

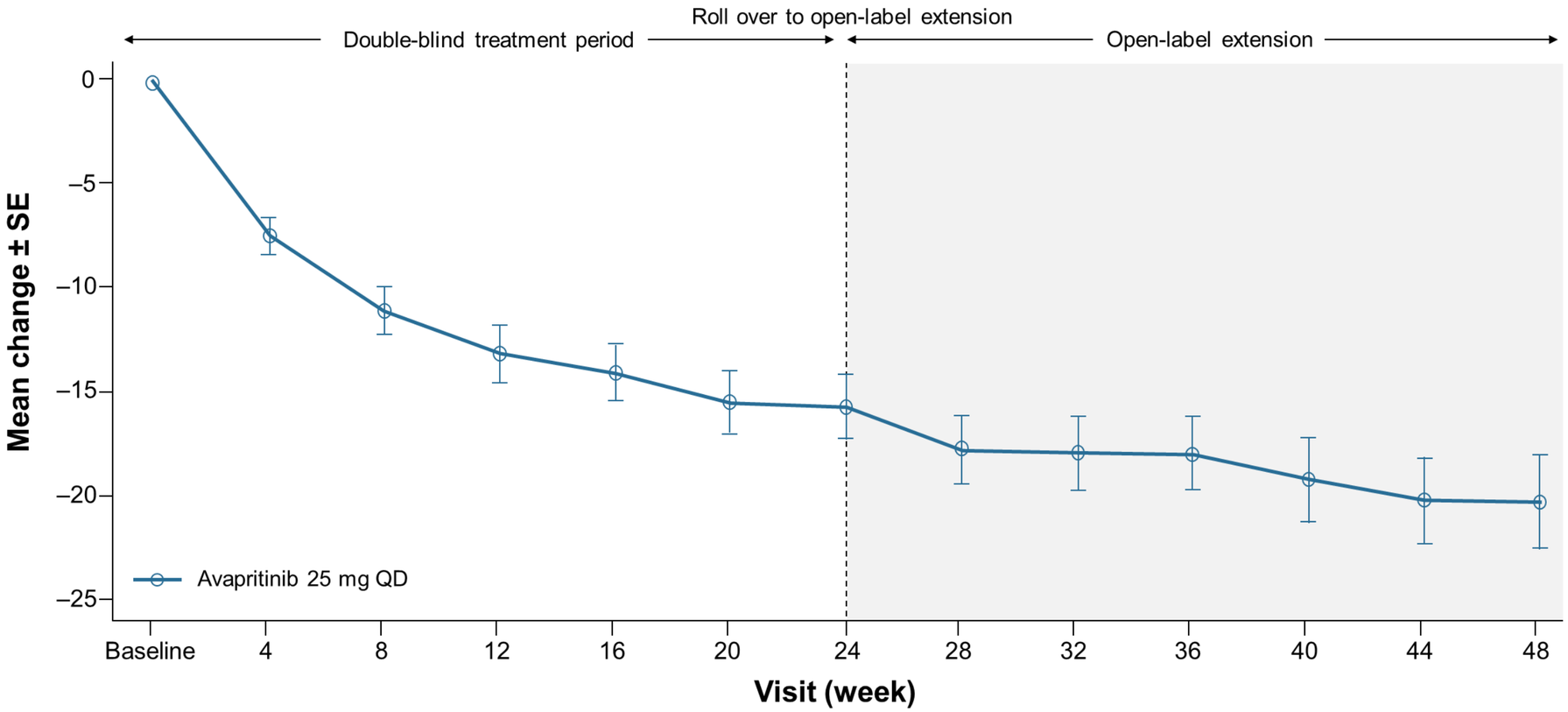
AYVAKIT showed rapid and sustained improvement on individual symptoms



1. Blueprint Medicines PIONEER data

AYVAKIT induced responses in patients that deepened over time

MEAN CHANGE IN TSS FOR AYVAKIT PATIENTS

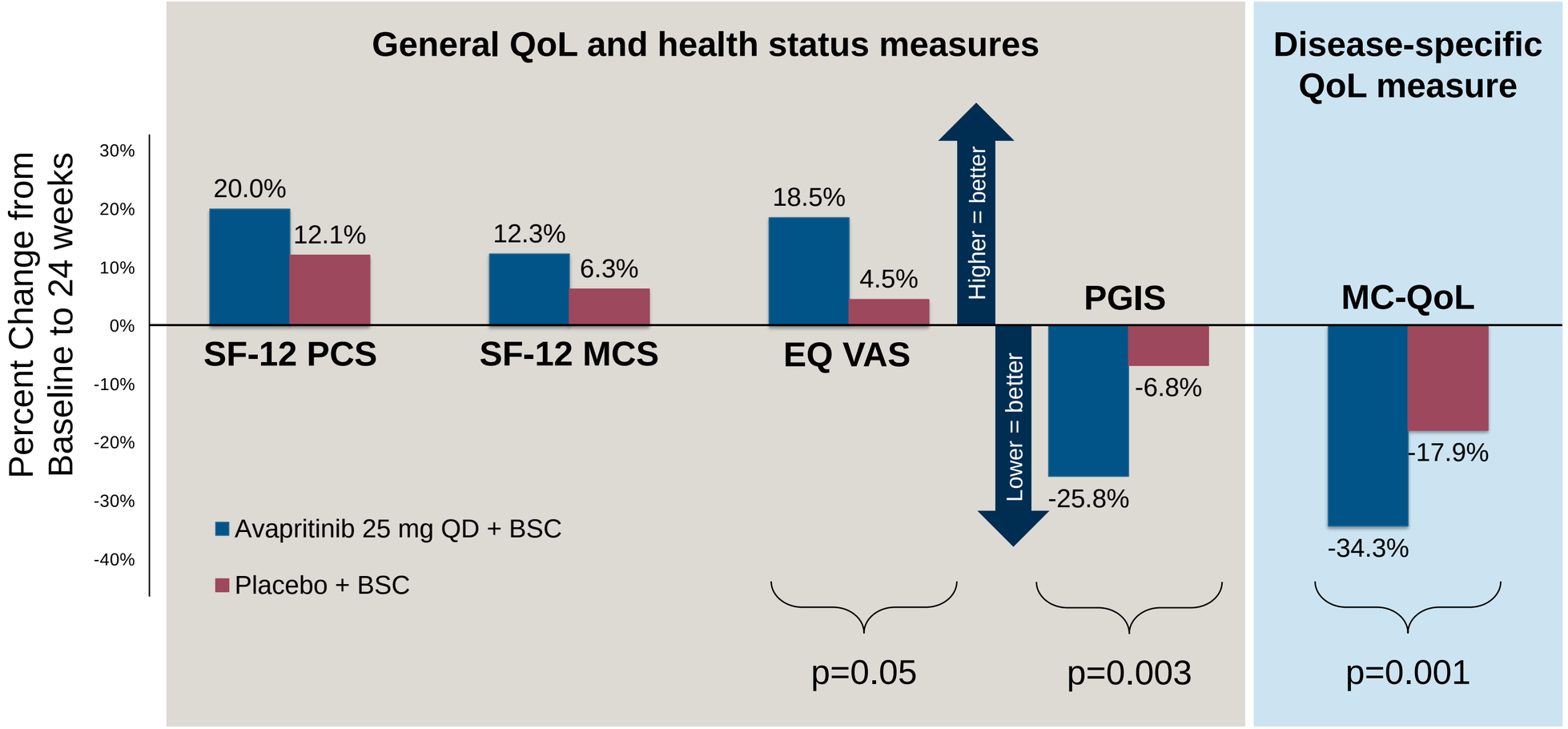


61% % with ≥30% TSS reduction at 48 weeks

39% % with ≥50% TSS reduction at 48 weeks

1. Blueprint Medicines PIONEER data

AYVAKIT demonstrated consistent impact on quality-of-life measures at 24 weeks



63% of AYVAKIT patients achieved a mild MC-QoL score by 48 weeks

1. Blueprint Medicines PIONEER data

Open-label PIONEER part 3 will continue to generate important data on AYVAKIT

LONG-TERM FOLLOW-UP ON:

- Symptom benefit over time
- Long-term safety and tolerability
- Quality of life impacts
- Reduction in polypharmacy

Randomized PIONEER part 2 was not designed to assess polypharmacy reduction, however changes observed in patients treated with AYVAKIT included:

24% reduced or completely discontinued best supportive care medications

26% reduced or discontinued cromolyn for gastrointestinal symptoms

1. Blueprint Medicines PIONEER data

Blueprint is the leader in SM, with AYVAKIT anchoring our franchise

- Statistically significant and clinically meaningful PIONEER data debuted at premiere allergy/immunology conference
- US and EMA regulatory submissions accepted
- May 22 US PDUFA date and launch readiness
- Practice-changing first-in-class systemic therapy for ISM upon approval

Q&A