Avapritinib in Systemic Mastocytosis
Focus: ISM/PIONEER data

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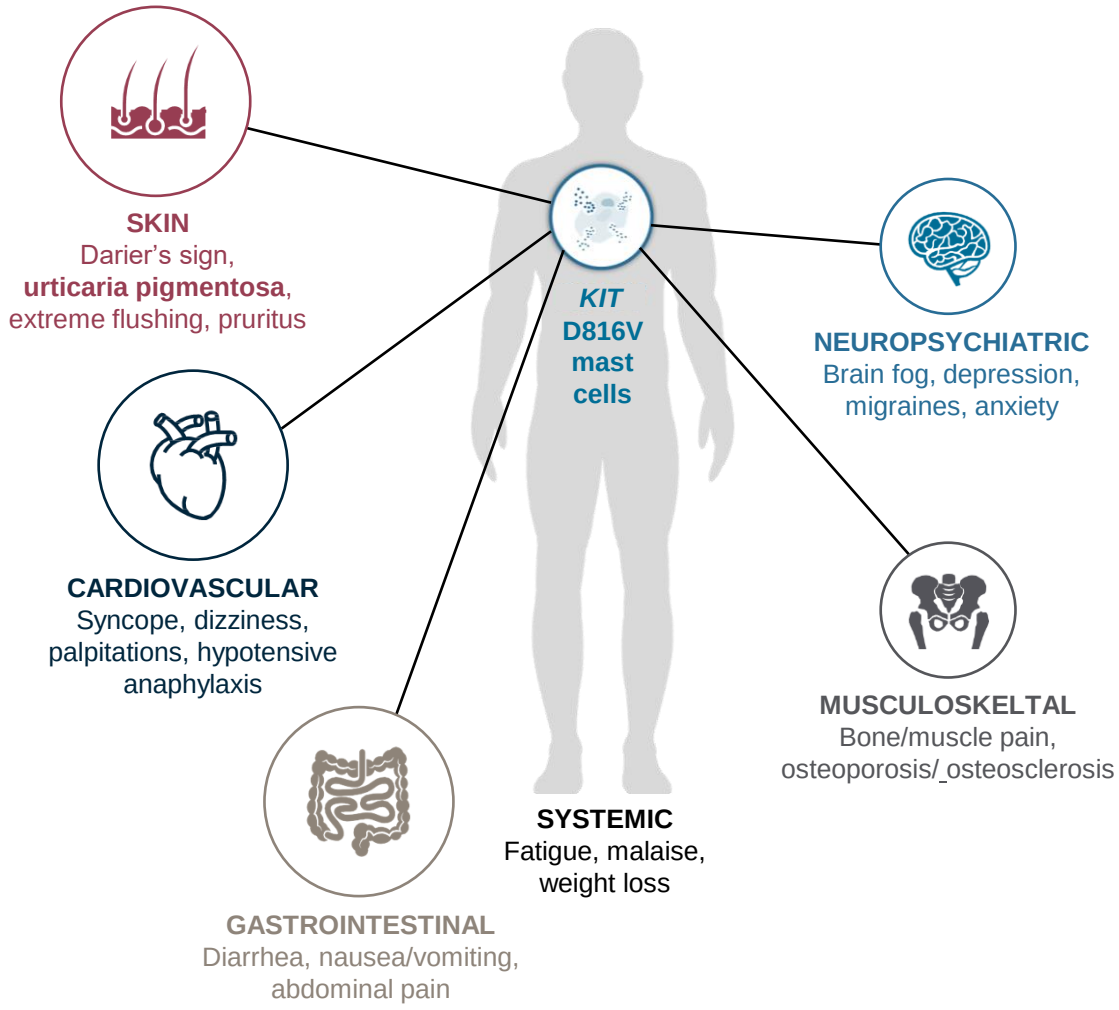
Focus:
Systemic Mastocytosis

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

1. Kristensen T et al. *J Mol Diagn*. 2011;13:180–8. **2.** Cohen SS et al. *Br J Haematol*. 2014;166:521–8. **3.** Arber DA et al. *Blood*. 2022;140:1200–1228. **4.** Mesa RA et al. *Cancer*. 2022;128:3691–3699. **5.** Hermine O et al. *PLoS One*. 2008;3:e2266. **6.** van Anrooij B. et al. *Allergy*. 2016;71:1585–1593. **7.** Hartmann K et al. *J Allergy Clin Immunol*. 2016;137:35–45. **8.** Akin C et al. *J Allergy Clin Immunol* 2022;149: 1912–8. **9.** Pardanani A. *Blood*. 2013;121:3085–94. **10.** Pardanani A. *Am J Hematol.* 2023 Jul;98(7):1097-1116.

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

Highly selective kinome profile[1]

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

Biochemical IC_{50} (nM)

	KIT D816V	KIT wild type
Avapritinib	0.27	73

KIT D816V IC_{50} = 0.27 nM0

Avapritinib kinase inhibitor activity

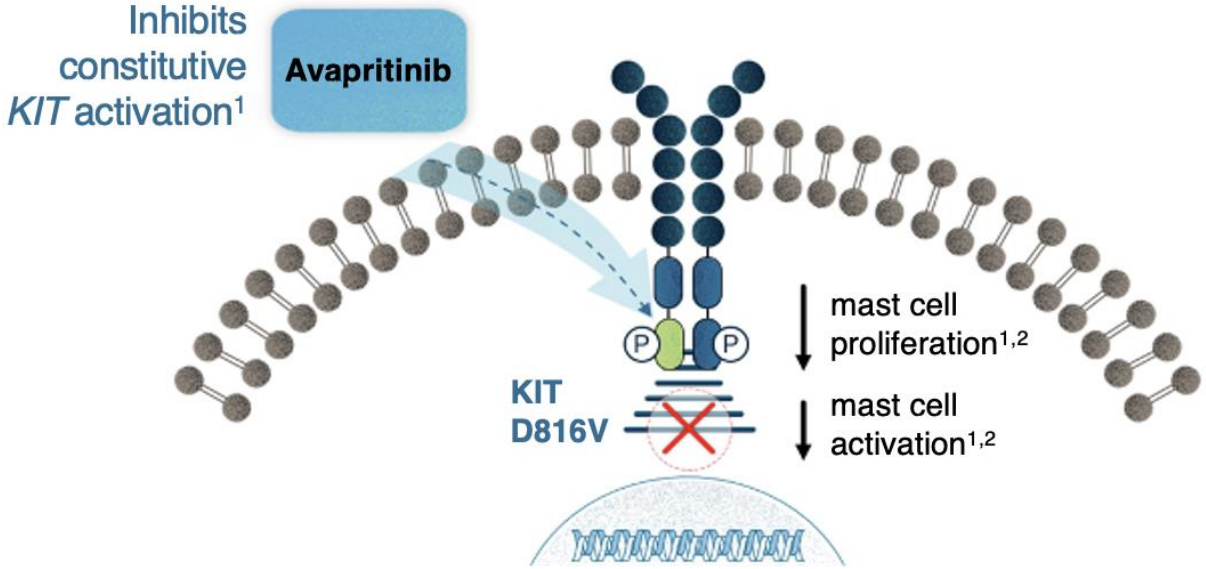


Figure based on: Gilreath et al. Clinical Pharmacology 2019[3]

nM = nanomolar concentration.
1. Evans EK et al. *Sci Transl Med*. 2017 Nov 1;9(414):eaao1690. **2.** Gotlib J et al. *Nat Med. 2021* Dec;27(12):2192–2199. **3.** Gilreath JA et al. *Clin Pharmacol*. 2019 Jul 10;11:77–92.

Focus:
Indolent Systemic Mastocytosis/PIONEER data

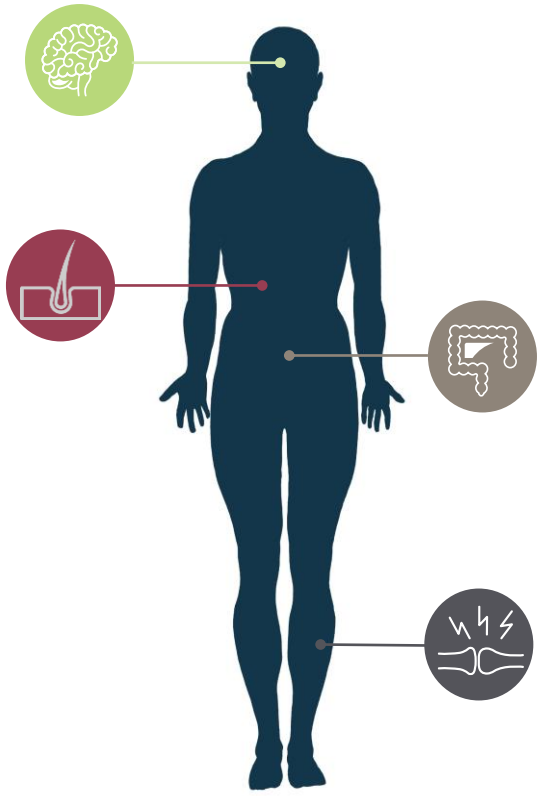
Focus:

Indolent Systemic Mastocytosis/PIONEER data

ISM-SAF: Validated symptom assessment tool specifically developed for evaluation of ISM symptomology[1–3]

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[1]



ISM Symptom Assessment Form (ISM-SAF)

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

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

1. Shields A et al. *Orphanet J Rare Dis*. 2023 (in press). **2.** Taylor F et al. *Orphanet J Rare Dis.* 2021;16:414. **3.** Padilla B et al. *Orphanet J Rare Dis*. 2021;16:434

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

Primary endpoint

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

Additional secondary endpoints

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

Biomarkers of mast cell burden
Key secondary endpoints

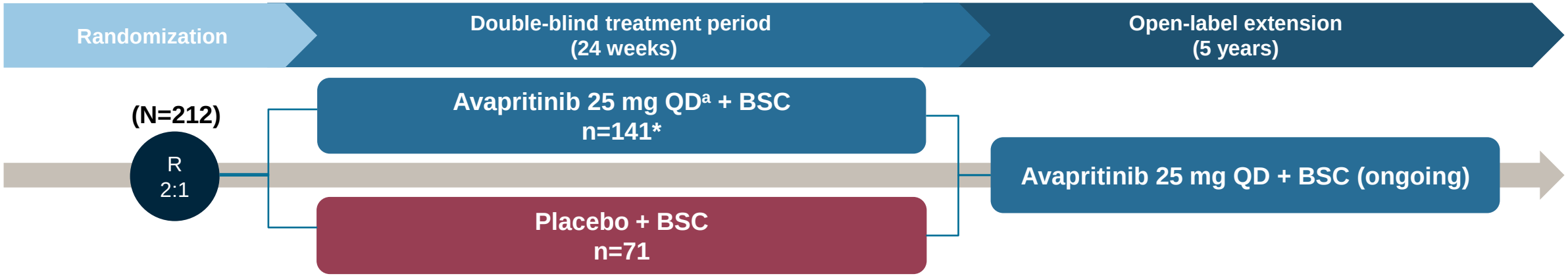
- ≥50% reduction in **serum tryptase** levels
- ≥50% reduction in ***KIT* D816V VAF** in peripheral blood (or below level of detection [<0.02%] for patients with a detectable mutation at baseline)
- ≥50% reduction in in bone marrow **mast cell aggregates**

Quality of life

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

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



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.

Based on Gotlib J et al. NEJM Evidence. 2023 Jun;2(6)

Baseline characteristics balanced between groups

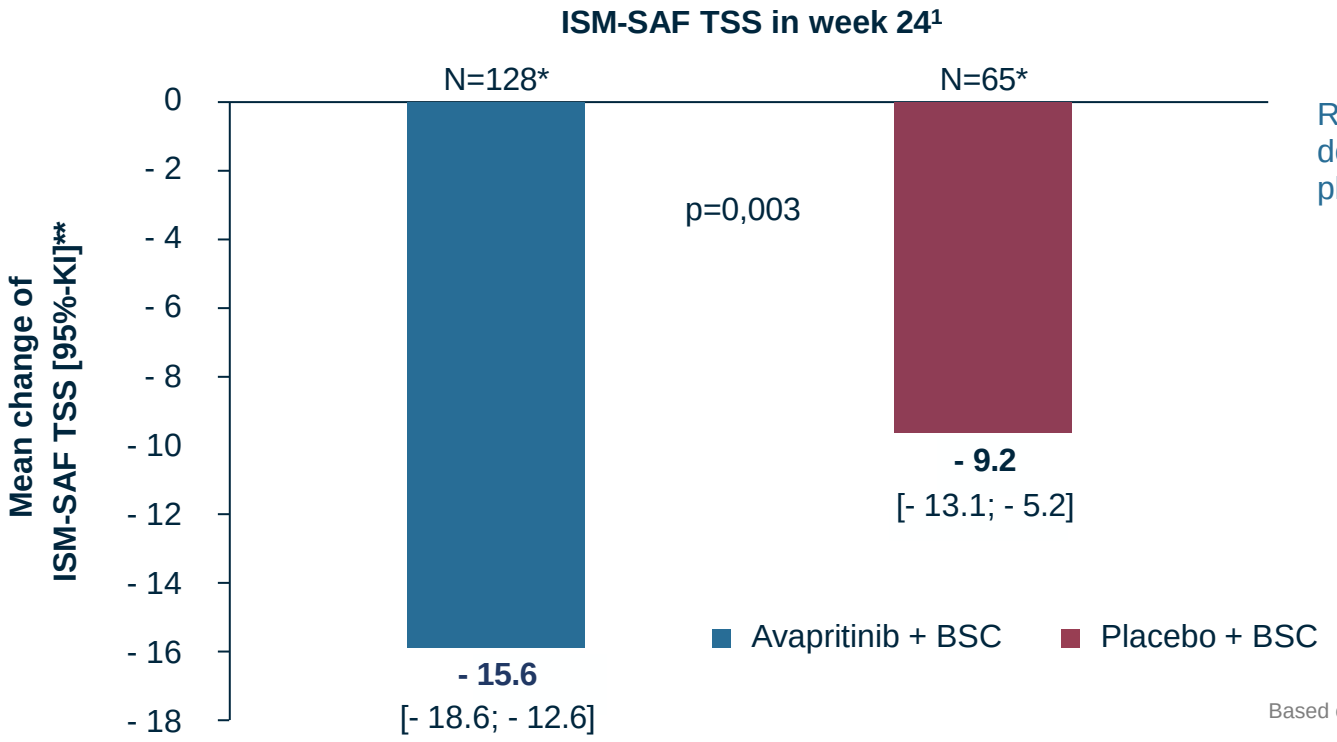
Patient demographic	Avapritinib 25 mg QD (n=141)	Placebo (n=71)
Age (years), median (range)	50.0 (18–77)	54.0 (26–79)
Female, n (%)	100 (70.9)	54 (76.1)
ISM symptom burden		
TSS score, mean (SD)	50.2 (19.1)	52.4 (19.8)
Most severe symptom score, mean (SD)	7.7 (1.7)	7.9 (1.7)
Mast cell burden		
Median 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.
Based on Gotlib J et al. NEJM Evidence. 2023 Jun;2(6)

Primary endpoint of the PIONEER study: Significant reduction in ISM-SAF TSS at 24 weeks

Patients treated with Avapritinib + BSC had a statistically significant improvement in total symptom score (ISM-SAF TSS) at week 24 compared to the control group (p=0.003)[1,2]

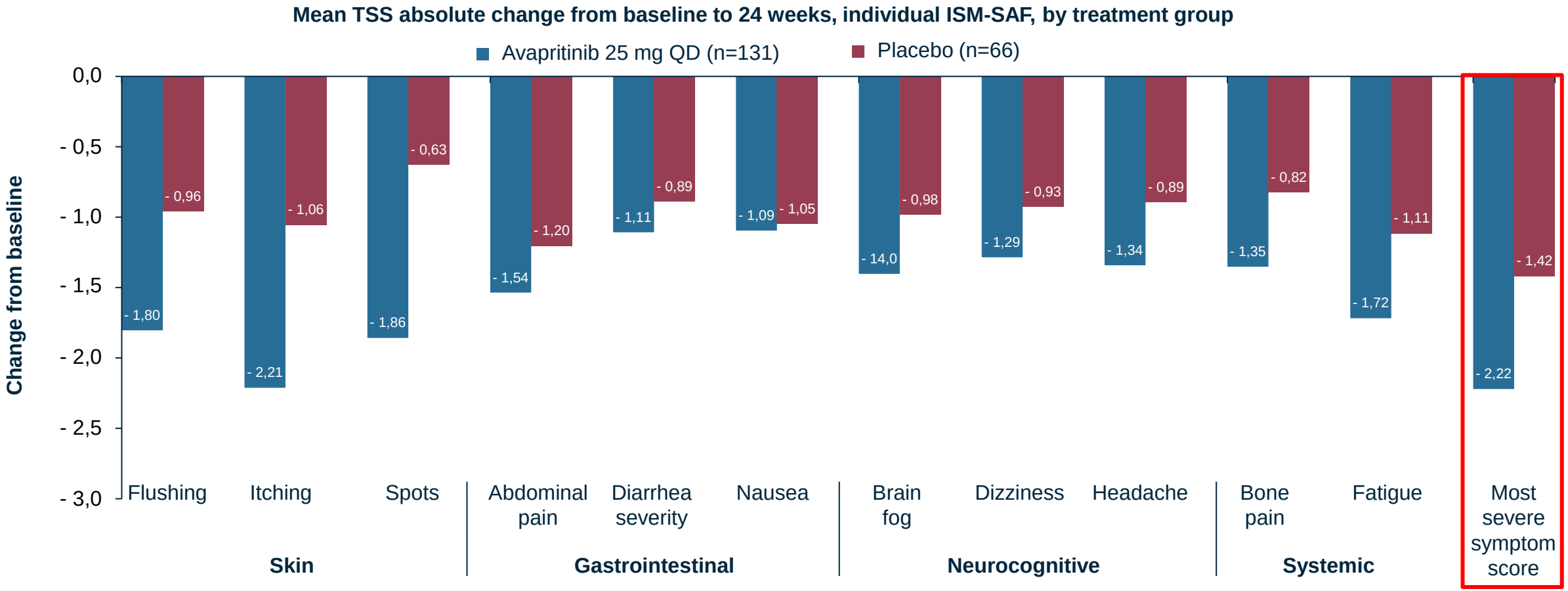


Results of the randomized, double-blind, placebo-controlled phase 2 study PIONEER[1]

Based on Gotlib J et al. NEJM Evidence. 2023 Jun;2(6)

Data cutoff June 23, 2022.
The calculation of the primary endpoint was based on the ITT population. Patients for whom both ISM-SAF TSS values (baseline and week 24) were not available, as well as patients taking high-dose glucocorticoids, were not included in the calculation. The number of patients for the statistical analysis was 128 for Avapritinib + BSC and 65 for placebo + BSC.[3]
****** The reduction in TSS is a result of the average decrease in all individual symptoms included in the ISM-SAF.
BSC = Best Supportive Care; **CI** = Confidence interval; **ISM-SAF** = Indolent Systemic Mastocytosis-Symptom Assessment Form (specific tool to investigate ISM symptoms; **ITT** = Intention-to-treat; **TSS** = Total Symptom Score (specific tool to investigate the total symptom score in mastocytosis).
1. Gotlib J et al. NEJM Evidence. 2023 Jun;2(6) **2.** Fachinformation AYVAKYT®, aktueller Stand **3.** AYVAKYT® EPAR Variation Assessment Report; Procedure No. EMEA/H/C/005208/II/0023; published 06/02/2024;

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

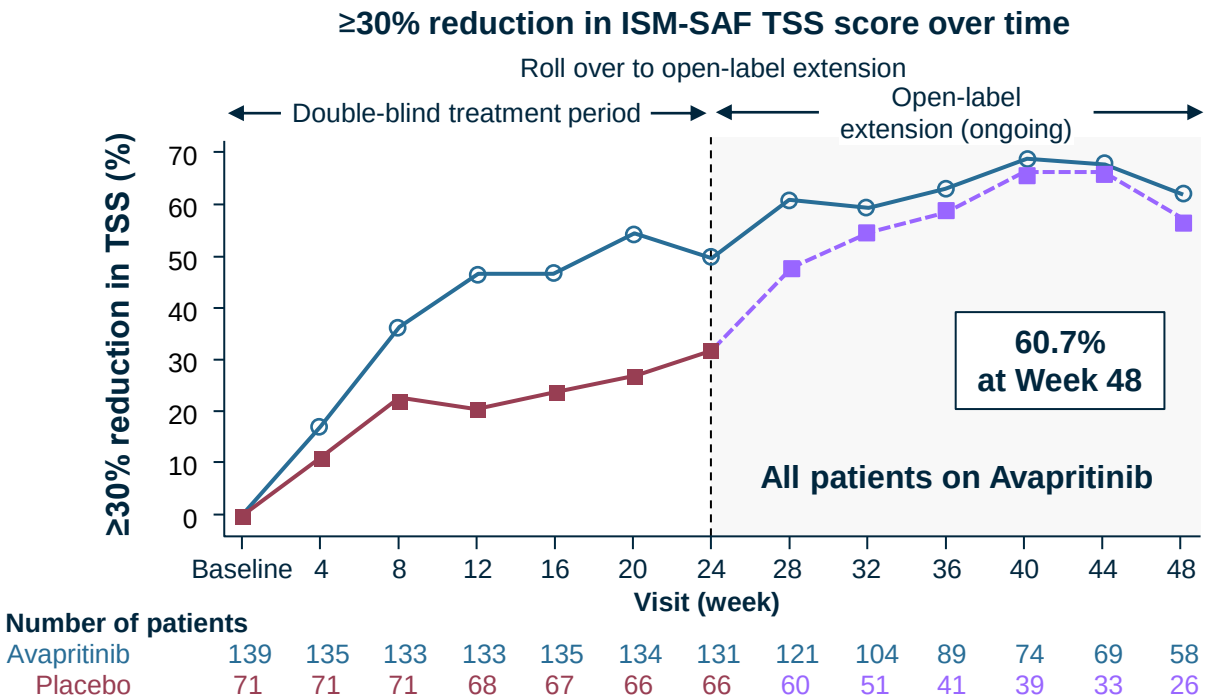


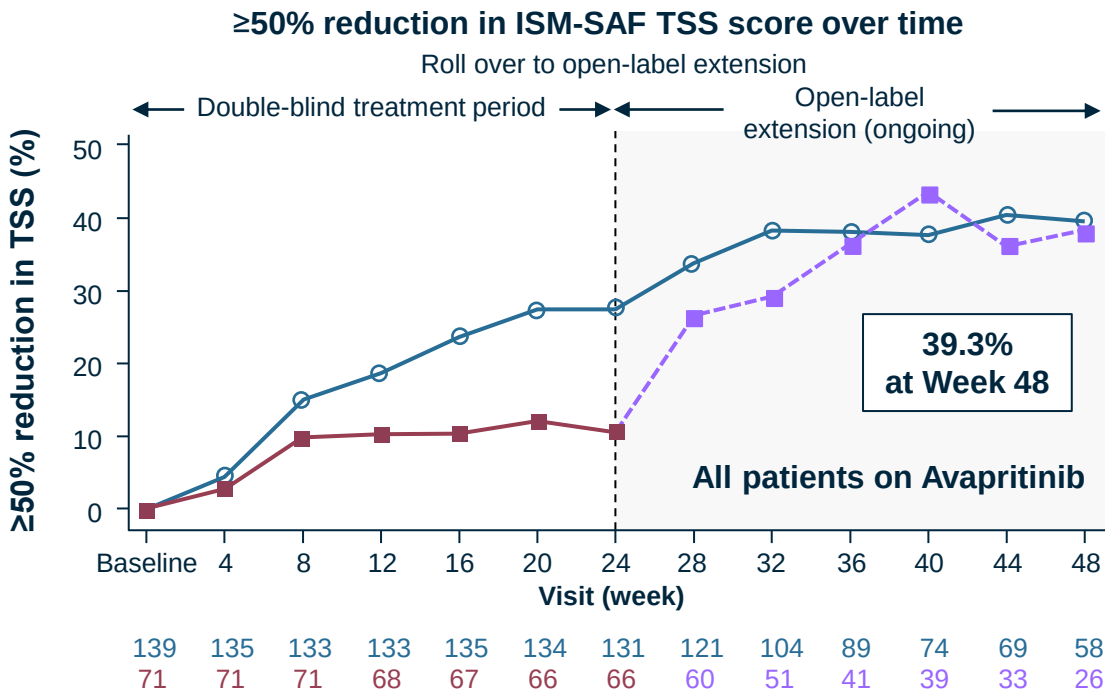
At Week 24	Avapritinib 25 mg QD (n=131)	Placebo (n=66)	P-value
Mean change in most severe symptom score (SD)	– 2.22 (2.30)	– 1.42 (1.88)	0.015

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

Castells M et al. AAAAI Annual Meeting, San Antonio, Texas, February 24-27, 2023; [Data not publicly available]

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





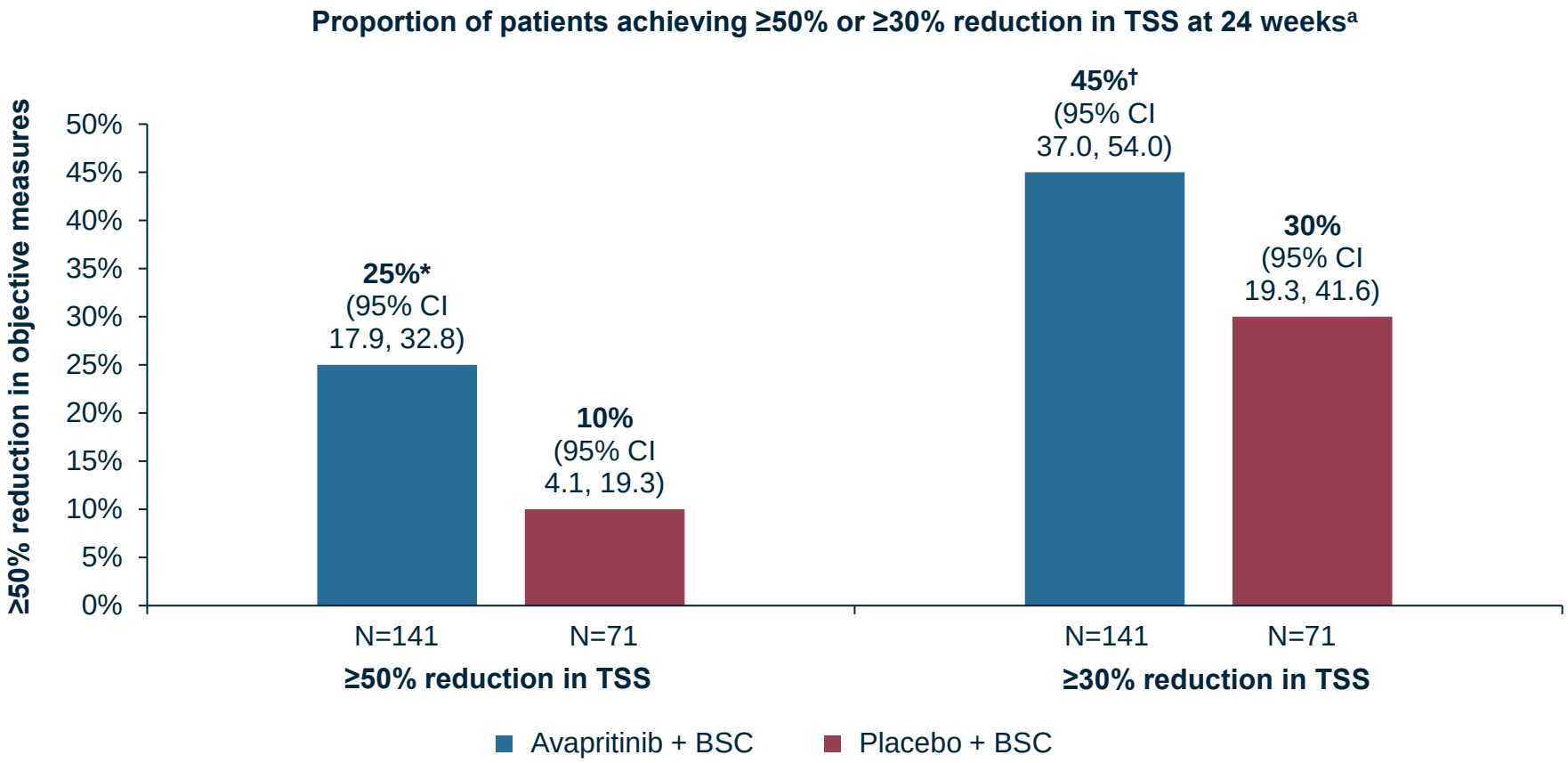
Treatment group: Avapritinib 25 mg QD; Placebo; Placebo group crossing over to receive Avapritinib 25 mg QD

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

Following completion of part 2, patients who continued to receive Avapritinib (for 48 weeks in total) and those who crossed over from placebo to Avapritinib (received 24 weeks of treatment) in part 3 were assessed for mean change in TSS and ≥50% and ≥30% reductions in TSS after another 24 weeks. A ≥30% reduction in TSS was determined to be a conservative estimate of a clinically important response for individual patients (i.e., meaningful within-person change) using an established score interpretation analysis such as anchor-based methods. The 30% reduction threshold aligns with the ISM treatment response criteria proposed by the European Competence Network on Mastocytosis and the American Initiative in Mast Cell Diseases. A ≥50% reduction in TSS, an even more conservative measure of treatment benefit, was also included as a secondary end point that is consistent with the symptom threshold chosen in previously conducted trials of symptom-driven diseases.
Castells M et al. AAAAI Annual Meeting, San Antonio, Texas, February 24-27, 2023; [Full publication of PIONEER available: Gotlib J et al. NEJM Evidence. 2023 Jun;2(6)]

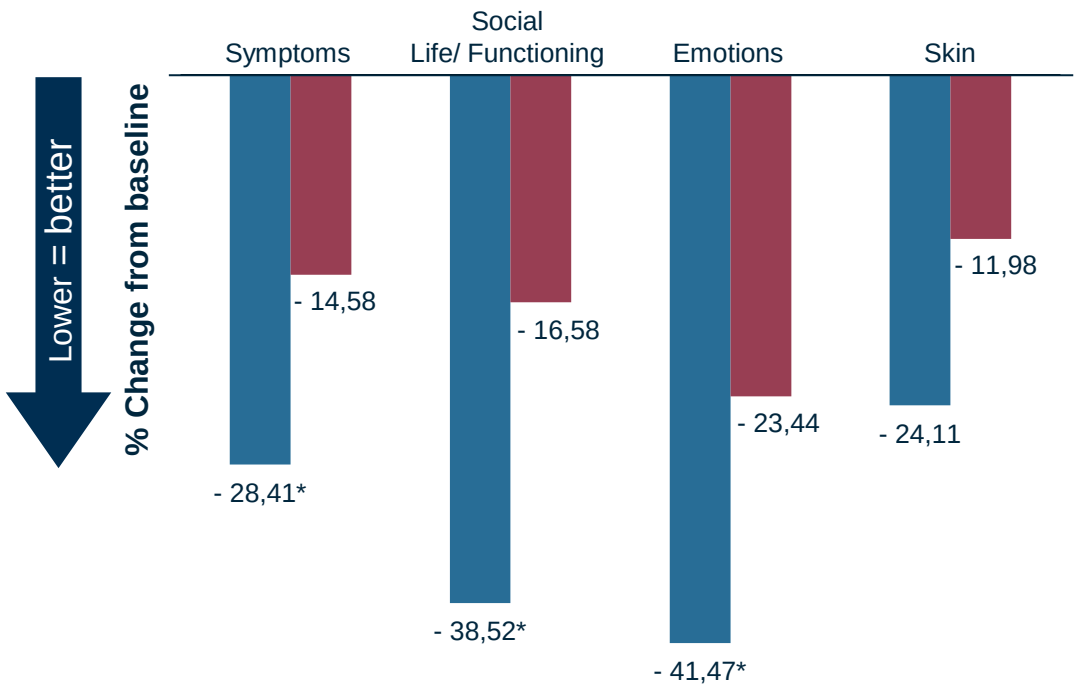
Avapritinib treatment demonstrated statistically significant improvement in secondary efficacy endpoints compared with placebo



Data cutoff June 23 2022.
***** 1-sided P=0.005; **†** 1-sided P=0.009; **a** ITT analysis: For patients with high-dose glucocorticoid use within 7 days before week 24 or greater than 14 consecutive days at any point from baseline to week 24, the week 24 score was considered missing for the primary efficacy analysis but was included in the figures of change o er time.
BSC = best supportive care; **TSS** = total symptom score.
A ≥30% reduction in TSS was determined to be a conservative estimate of a clinically important response for individual patients (i.e., meaningful within-person change) using an established score interpretation analysis such as anchor-based methods. The 30% reduction threshold aligns with the ISM treatment response criteria proposed by the European Competence Network on Mastocytosis and the American Initiative in Mast Cell Diseases. A ≥50% reduction in TSS, an even more conservative measure of treatment benefit, was also included as a secondary end point that is consistent with the symptom threshold chosen in previously conducted trials of symptom-driven diseases.
Based on Fachinformation Ayvakyt®, aktueller Stand.

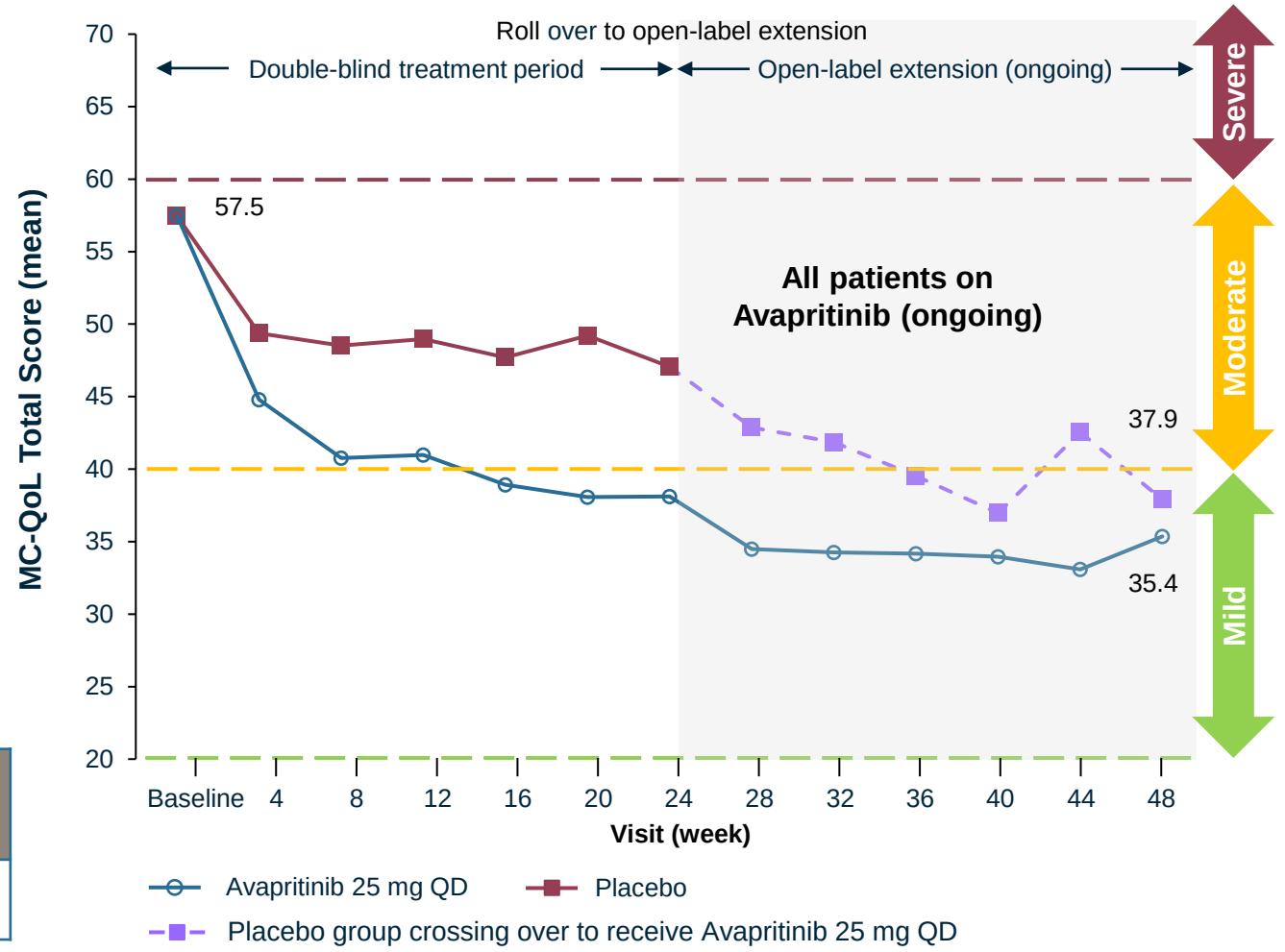
Avapritinib demonstrated sustained improvement in MC-QoL *versus* placebo, an established and validated disease-specific QoL measure

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

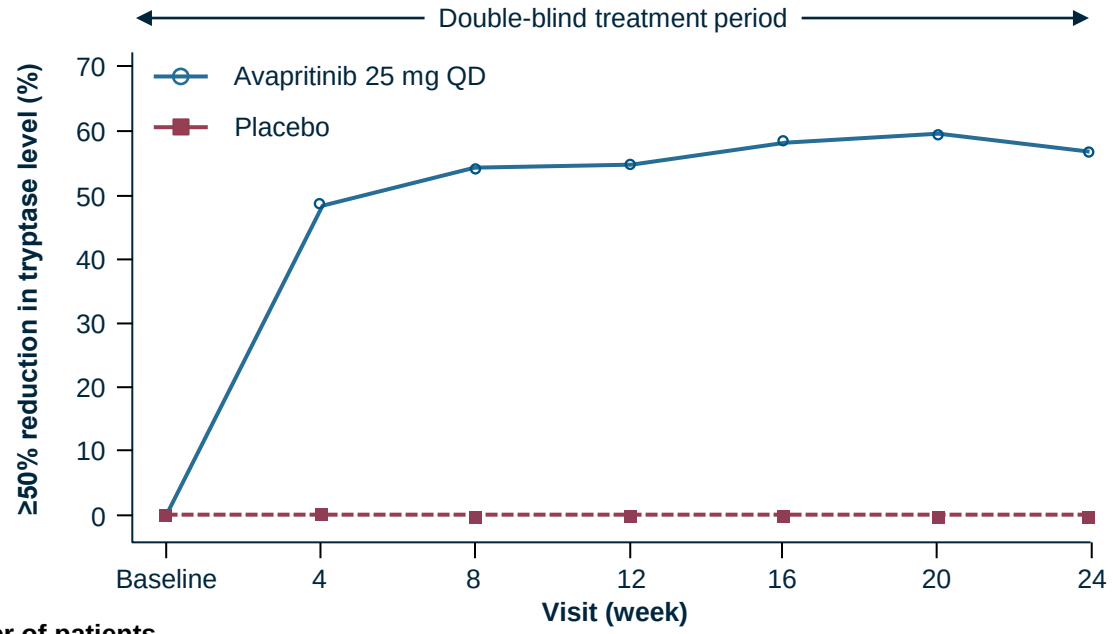


* p ≤ 0.05.
ITT = intent-to-treat.
Modified from Gotlib J et al. NEJM Evidence. 2023 Jun;2(6)

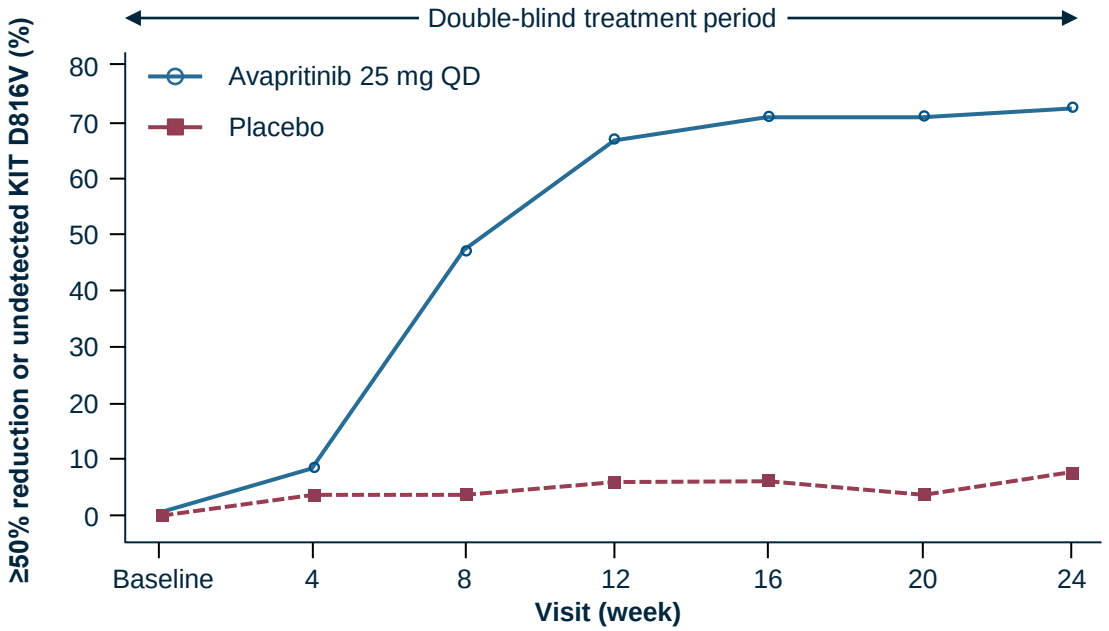
Rapid and sustained reductions in biomarkers of mast cell burden in Avapritinib-treated patients *versus* placebo

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
Placebo	71	66	62	61	60	62	64

Avapritinib	118	110	113	109	107	104	109
Placebo	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

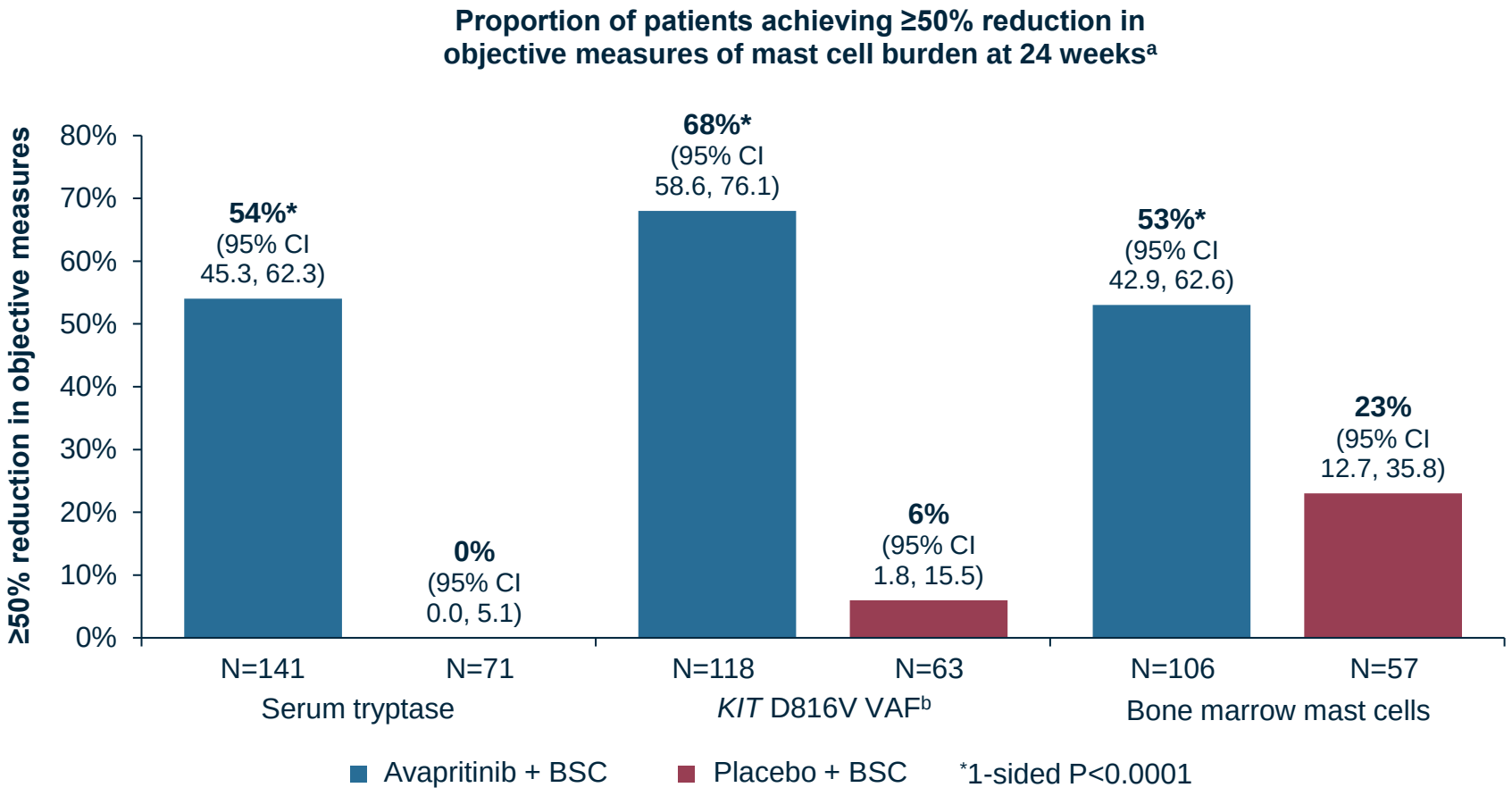
At Week 24	Avapritinib 25 mg QD (n=141)	Placebo (n=71)	P-value
Proportion of patients with **≥50% reduction in *KIT* D816V VAF** (95% CI)	67.8% (58.6–76.1)	6.3% (1.8–15.5)	<0.0001

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.

Maurer M et al. AAAAI Annual Meeting, San Antonio, Texas, February 24-27, 2023 [Full publication of PIONEER available: Gotlib J et al. NEJM Evidence. 2023 Jun;2(6)]

Avapritinib treatment demonstrated statistically significant improvement for key secondary efficacy endpoints compared with placebo



Data cutoff June 23 2022.
a ITT analysis: For patients with high-dose glucocorticoid use within 7 days before week 24 or greater than 14 consecutive days at any point from baseline to week 24, the week 24 score was considered missing for the primary efficacy analysis but was included in the figures of change over time. **b** Percent of patients with ≥50% reduction in peripheral blood *KIT* D816V VAF or undetectable.
BSC = best supportive care; **VAF** = variant allele fraction.
Based on Fachinformation Ayvakyt®, aktueller Stand

Adverse reactions

Adverse reactions*	Avapritinib 25 mg QD (N=141) Any grade	Grade ≥3
Peripheral edema,[a] %	12.1	0
Flushing, %	9.2	1.4
Face edema, %	7.1	0
Blood alkaline phosphatase increased, %	6.4	0.7
Insomnia, %	5.7	0
Photosensitivity reaction, %	2.8	0

Adapted from Fachinformation Ayvakyt®, aktueller Stand

* Adverse reactions that occurred in ≥5% of patients in Part 2 of the PIONEER study

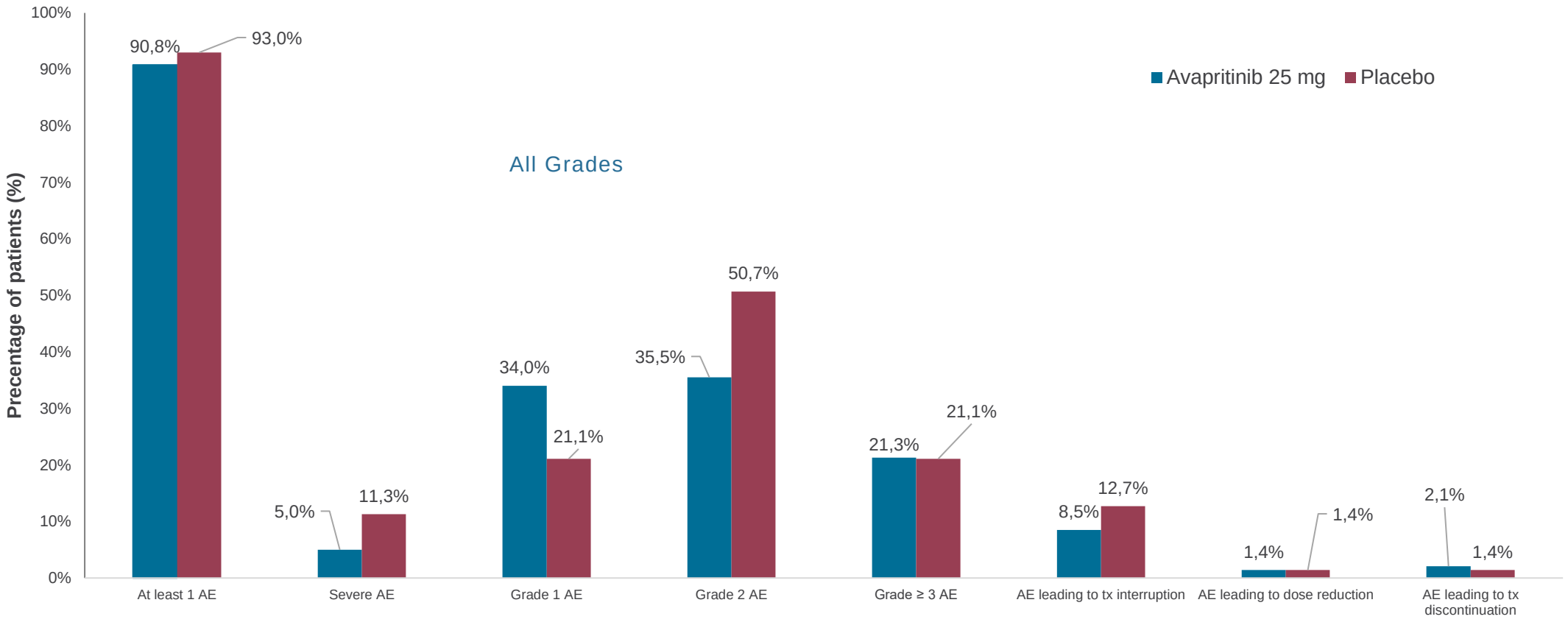
At the recommended dose of 25 mg once daily** in Part 2 of PIONEER:

- The most common adverse reaction in the Avapritinib group was **peripheral oedema (12%)**
- The majority of oedema adverse reactions were **Grade 1 (94% for peripheral oedema, 90% for face oedema);** none were Grade ≥3 or led to treatment discontinuation
- **No serious adverse reactions or fatal adverse reactions** occurred in 141 patients receiving Avapritinib
- **Treatment discontinuation** due to adverse reactions occurred in **<1% of patients** receiving Avapritinib

****** the recommended dose of 25 mg Avapritinib once daily
a peripheral edema (including edema peripheral and peripheral swelling)
BSC = best supprtive care; **ISM** = indolent systemic mastocytosis
Fachinformation Ayvakyt®, aktueller Stand

Avapritib was well tolerated and the rate of adverse events was generally low

Treatment discontinuation due to adverse events occurred in ~2% of patients receiving Avapritinib



Tx = therapy.

Based on: Gotlib J et al. Poster Number 1017, Presented at the European Hematology Association Annual Meeting, Frankfurt & Virtual, June 8–15, 2023 [Data not publicly available]

Focus: Skin data

Focus:
Skin data

Comprehensive assessment of skin changes from baseline to Week 24

ISM-SAF
(completed by all patients)

- Daily PRO assessment of 11 ISM related symptoms
- Each evaluated on a 0–10 scale (no symptoms – worst imaginable)
- Skin domain is comprised of spot, flushing and itching for a total scale of 0–30

Skin photographs
(Avapritinib n=74, placebo n=37)

- Optional, taken at baseline and every 12 weeks
- Photographs assessed by
  - *Computer-generated algorithm* - calculated affected surface area
  - *Blinded SAC*

Skin biopsies
(Avapritinib n=107, placebo n=60)

- Performed in patients with mastocytosis in skin at baseline and at Week 24
- Quantification of mast cell infiltrates was performed by central pathology
- Mast cell number and immunophenotype in skin biopsies were assessed via light microscopy and immunohistochemistry

MC-QoL = Mastocytosis Quality of Life questionnaire; **PRO** = patient-reported outcome; **SAC** = skin assessment committee.
Maurer M et al. AAAAI Annual Meeting, San Antonio, Texas, February 24-27, 2023 [Data not publicly available]

Blinded SAC evaluation of skin photographs

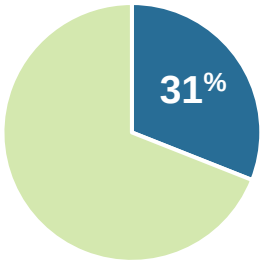
Blinded SAC determined:

- Most affected region at baseline
- Color change over time

Computer-generated algorithm for each patient

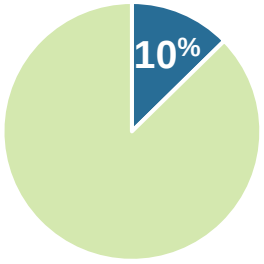
- Affected surface area was followed with computer generated detection method
- Number of lesions, fractional area, and percent fractional area were determined

Baseline



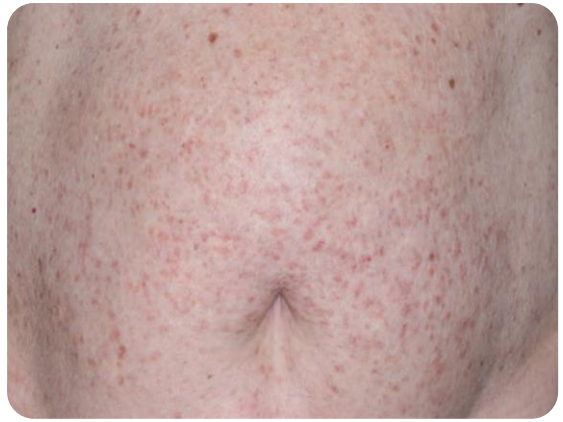
Affected surface area

On study

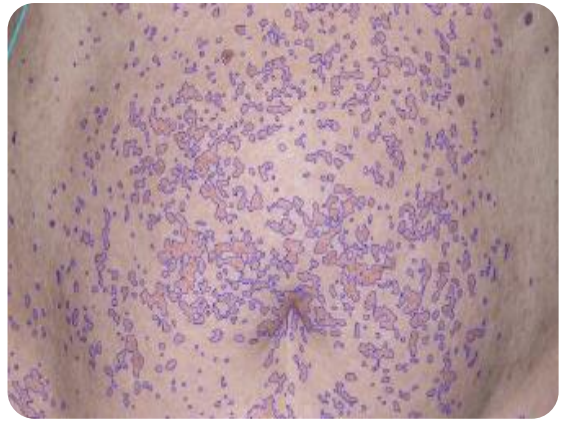


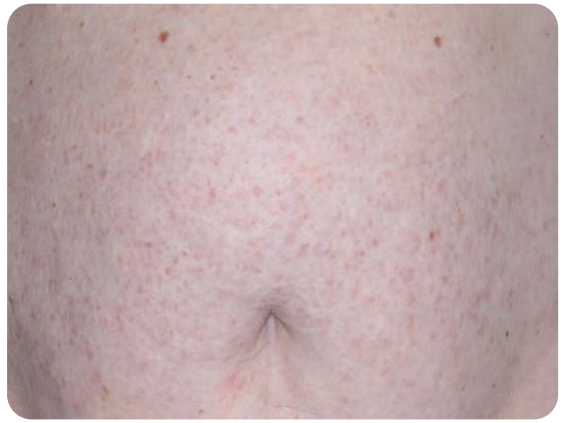
Affected surface area

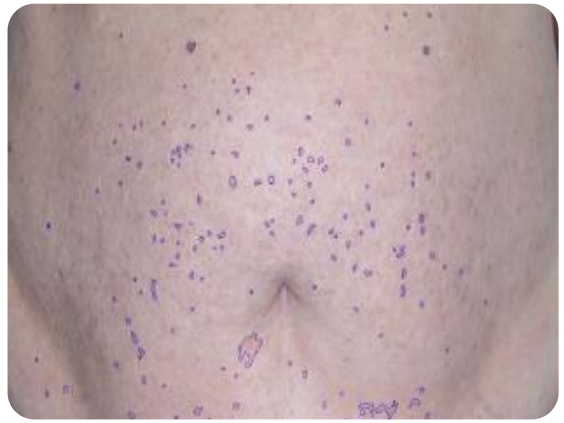
Photograph



Computer detection







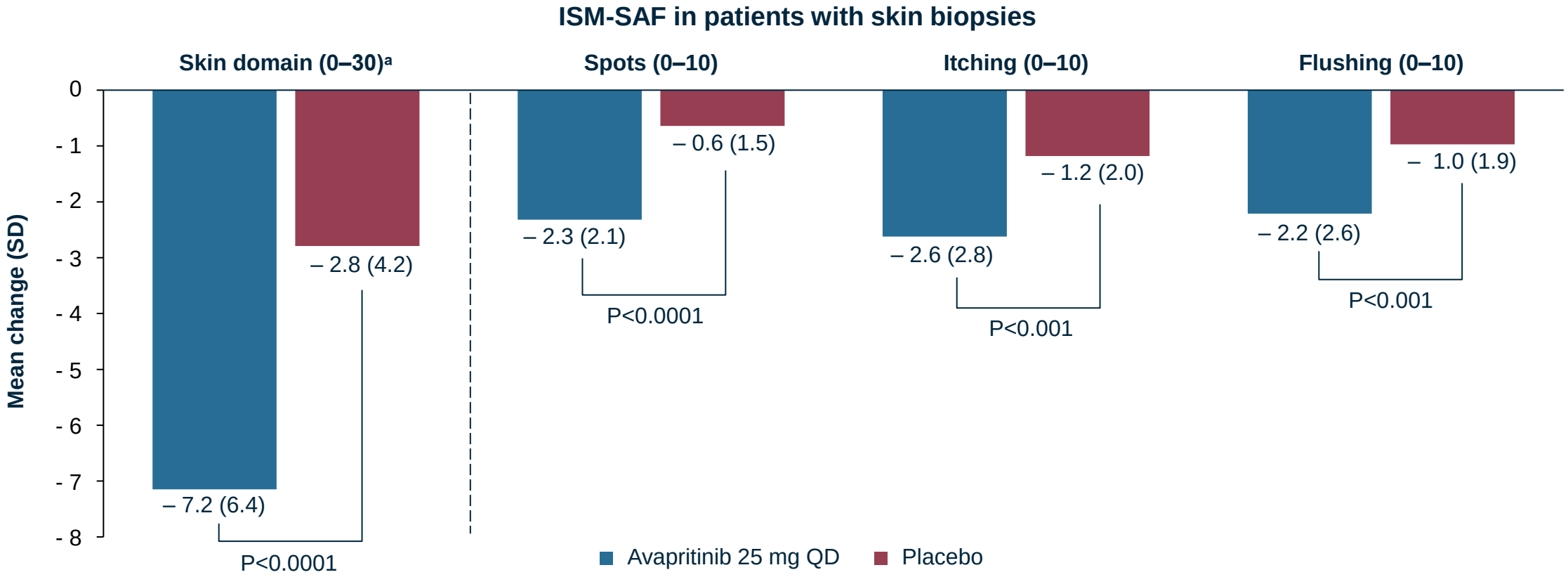
Patient permission granted for use of photos

SAC = skin assessment committee.

Maurer M et al. AAAAI Annual Meeting, San Antonio, Texas, February 24-27, 2023 [Data not publicly available]

Significant improvements in ISM-SAF patient-reported skin domain, individual skin symptoms, and QoL in Avapritinib-treated patients

- In the majority of patients, the most severe symptom domain at baseline was the skin domain
- A correlation was observed between ISM-SAF skin domain score change from baseline and MC-QoL total score change from baseline

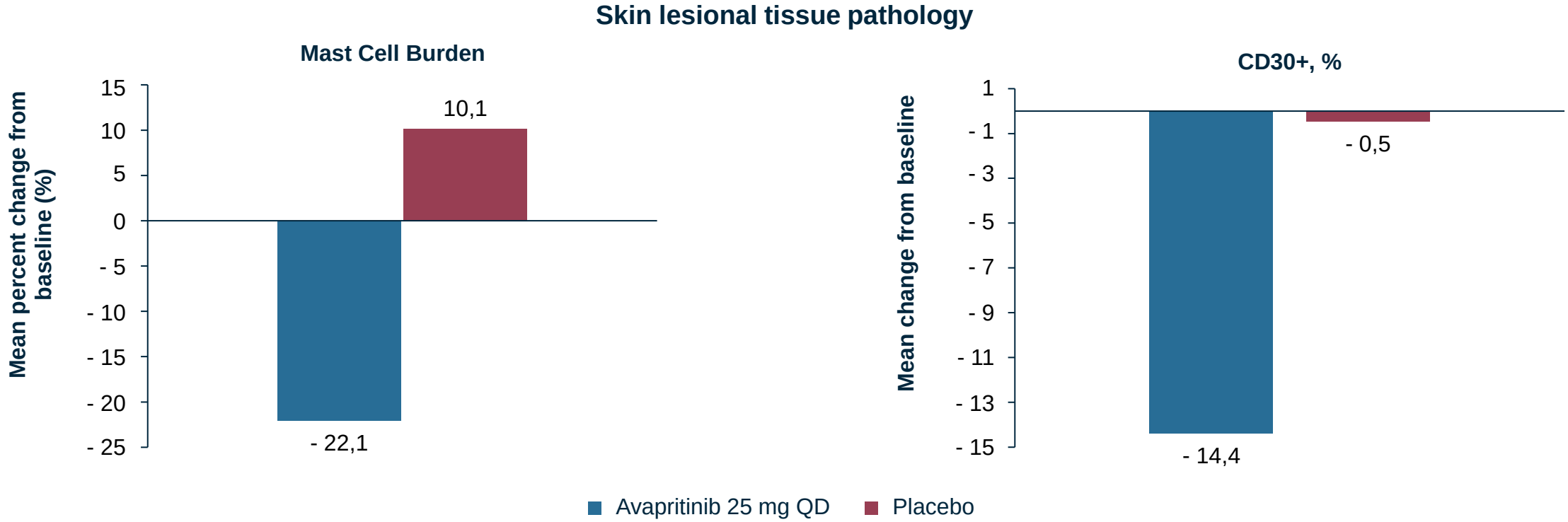


a Skin domain scores include the total score for spot, itching, and flushing severity.

Maurer M et al. AAAAI Annual Meeting, San Antonio, Texas, February 24-27, 2023 [Data not publicly available]

Marked reduction of mast cell burden and CD30+ in skin lesions with Avapritinib-treatment

- Mean percent change (SD) of mast cell burden decreased at Week 24 with Avapritinib (− 22.1% [106], n=87) but increased with placebo (10.1% [121], n=49)
- Avapritinib significantly decreased CD30+ mast cell proportion in skin lesions at Week 24 *versus* placebo (− 14.4% vs − 0.5%; P=0.0015)



Maurer M et al. AAAAI Annual Meeting, San Antonio, Texas, February 24-27, 2023 [Data not publicly available]

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
- The most common adverse reaction in the Avapritinib group was peripheral oedema (12%)
- 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

Pflichttext Ayvakyt®

AYVAKYT® 25 mg Filmtabletten / AYVAKYT® 50 mg Filmtabletten / AYVAKYT® 100 mg Filmtabletten / AYVAKYT® 200 mg Filmtabletten / AYVAKYT® 300 mg Filmtabletten
Wirkstoff: Avapritinib

▼Dieses Arzneimittel unterliegt einer zusätzlichen Überwachung. Dies ermöglicht eine schnelle Identifizierung neuer Erkenntnisse über die Sicherheit. Angehörige von Gesundheitsberufen sind aufgefordert, jeden Verdachtsfall einer Nebenwirkung zu melden. Hinweise zur Meldung von Nebenwirkungen, siehe Abschnitt 4.8 der Fachinformation.
Qualitative und quantitative Zusammensetzung:
AYVAKYT 25 mg Filmtabletten: Jede Filmtablette enthält 25 mg Avapritinib.
AYVAKYT 50 mg Filmtabletten: Jede Filmtablette enthält 50 mg Avapritinib.
AYVAKYT 100 mg Filmtabletten: Jede Filmtablette enthält 100 mg Avapritinib.
AYVAKYT 200 mg Filmtabletten: Jede Filmtablette enthält 200 mg Avapritinib.
AYVAKYT 300 mg Filmtabletten: Jede Filmtablette enthält 300 mg Avapritinib.
Vollständige Auflistung der sonstigen Bestandteile: *Tablettenkern:* Mikrokristalline Cellulose, Copovidon, Croscarmellose-Natrium, Magnesiumstearat; *Tablettenüberzug:* Talkum, Macrogol 3350, Poly(vinylalkohol), Titandioxid (E171); *Druckfarbe (nur bei 100 mg, 200 mg und 300 mg Filmtabletten):* Schellack, verestert (20 % verestert), Brillantblau FCF (E133), Titandioxid (E171), Eisen(II,III)-oxid (E172), Propylenglycol.
Anwendungsgebiete:
Inoperabler oder metastasierter gastrointestinaler Stromatumor (GIST)
AYVAKYT ist als Monotherapie zur Behandlung erwachsener Patienten mit inoperablen oder metastasierten gastrointestinalen Stromatumoren (GIST), die die Thrombozyten-Wachstumsfaktor-Rezeptor-alpha (PDGFRA)-D842V-Mutation aufweisen, indiziert.
Fortgeschrittene systemische Mastozytose (AdvSM)
AYVAKYT ist als Monotherapie zur Behandlung erwachsener Patienten mit aggressiver systemischer Mastozytose (ASM), systemischer Mastozytose mit assoziierter hämatologischer Neoplasie (SM-AHN) oder Mastzellleukämie (MCL) nach zumindest einer systemischen Therapie indiziert.
Indolente systemische Mastozytose (ISM)
AYVAKYT ist zur Behandlung erwachsener Patienten mit indolenter systemischer Mastozytose (ISM) mit mittelschweren bis schweren Symptomen indiziert, bei denen mit einer symptomatischen Behandlung keine ausreichende Kontrolle erzielt werden kann (siehe Abschnitt 5.1 der Fachinformation).
Gegenanzeigen: Überempfindlichkeit gegen den Wirkstoff oder einen der sonstigen Bestandteile.

Nebenwirkungen:
Inoperable oder metastasierte GIST: *sehr häufig:* Anämie, erniedrigte Leukozytenzahl, erniedrigte Neutrophilenzahl, verminderter Appetit, eingeschränktes Erinnerungsvermögen, kognitive Störung, Schwindelgefühl, Auswirkungen auf den Geschmack, verstärkte Tränensekretion, Abdominalschmerz, Erbrechen, Diarrhoe, Übelkeit, Trockenheit, gastro-ösophageale Refluxkrankheit, Hyperbilirubinämie, Änderungen der Haarfarbe, Ausschlag, Ödem, Ermüdung, erhöhte Transaminasen; *häufig:* Konjunktivitis, Thrombozytopenie, erniedrigte Lymphozytenzahl, Hypophosphatämie, Hypokaliämie, Hypomagnesiämie, Hyponatriämie, Dehydratation, Hypoalbuminämie, Hypokalzämie, Verwirrtheitszustand, Depression, Angst, Schlaflosigkeit, intrakranielle Blutung, geistige Beeinträchtigungen, periphere Neuropathie, Somnolenz, Aphasie, Hypokinesie, Kopfschmerzen,

Gleichgewichtsstörung, Sprechstörung, Tremor, okuläre Blutung, verschwommenes Sehen, Bindehautblutung, Photophobie, Vertigo, Hypertonie, Pleuraerguss, Dyspnoe, Nasenverstopfung, Husten, Gastrointestinalblutung, Aszites, Obstipation, Dysphagie, Stomatitis, Flatulenz, Hypersalivation, palmar-plantares Erythrodysästhesiesyndrom, Lichtempfindlichkeitsreaktion, Hauthypopigmentierung, Pruritus, Alopezie, Myalgie, Arthralgie, Rückenschmerzen, Muskelspasmen, akute Nierenschädigung, erhöhtes Kreatinin im Blut, Hämaturie, Asthenie, Fieber, Unwohlsein, Kältegefühl, Elektrokardiogramm QT verlängert, erhöhte Kreatinphosphokinase im Blut, erniedrigtes Gewicht, erhöhtes Gewicht, erhöhte Laktatdehydrogenase im Blut; *gelegentlich:* Tumorblutung, Enzephalopathie, Perikarderguss, Leberblutung.
Fortgeschrittene systemische Mastozytose: *sehr häufig:* Thrombozytopenie, Anämie, Neutropenie, Auswirkungen auf den Geschmack, kognitive Störung, Diarrhoe, Übelkeit, Änderungen der Haarfarbe, Ödem, Ermüdung; *häufig:* Leukopenie, Verwirrtheitszustand, Kopfschmerzen, eingeschränktes Erinnerungsvermögen, Schwindelgefühl, periphere Neuropathie, intrakranielle Blutung, verstärkte Tränensekretion, Epistaxis, Pleuraerguss, Erbrechen, gastro-ösophageale Refluxkrankheit, Aszites, Trockenheit, Obstipation, Abdominalschmerz, Gastrointestinalblutung, Hyperbilirubinämie, Ausschlag, Alopezie, Arthralgie, Schmerz, erhöhtes Gewicht, erhöhte Alkalische Phosphatase im Blut, erhöhte Transaminasen, Elektrokardiogramm QT verlängert, Kontusion; *gelegentlich:* Perikarderguss, Lichtempfindlichkeitsreaktion, akute Nierenschädigung.
Indolente systemische Mastozytose: *sehr häufig:* Peripheres Ödem; *häufig:* Insomnie, Flush, Lichtempfindlichkeitsreaktion, Gesichtsödem, erhöhte Alkalische Phosphatase im Blut.
Verkaufsabgrenzung: Deutschland: Verschreibungspflichtig; Österreich: Rezept- und apothekenpflichtig, wiederholte Abgabe verboten.
Pharmakotherapeutische Gruppe: Antineoplastische Mittel, Proteinkinase-Inhibitoren, ATC-Code: L01EX18.
Pharmazeutischer Unternehmer/Inhaber der Zulassung: Blueprint Medicines (Netherlands) B.V., Gustav Mahlerplein 2, 1082 MA Amsterdam, Niederlande.
Weitere Informationen: Ausführliche Informationen zu Warnhinweisen und Vorsichtsmaßnahmen für die Anwendung, Wechselwirkungen, Schwangerschaft und Stillzeit sowie Nebenwirkungen entnehmen Sie bitte der veröffentlichten Fachinformation (Zusammenfassung der Merkmale des Arzneimittels). AYV-101