BRIDGE^{SM} BUILDING BRIDGES

BETWEEN TREATMENT CENTERS & COMMUNITY PRACTICES: REDUCING KNOWLEDGE GAPS IN MANAGEMENT OF SYSTEMIC MASTOCYTOSIS

Patient Resources

National Comprehensive Cancer Network®

NCCN Guidelines for Patients®
https://www.nccn.org/patients/guidelines/content/PDF/systemic-mastocytosis-patient-guideline.pdf

The Mast Cell Disease Society

The Mast Cell Disease Society
https://tmsforacure.org/

NIH NCATS | GARD Genetic and Rare Diseases Information Center

Genetic and Rare Diseases Information Center
https://rarediseases.info.nih.gov/

NORD® National Organization for Rare Disorders

National Organization for Rare Disorders
https://rarediseases.org/

American Initiative in Mast Cell Diseases

American Initiative in Mast Cell Diseases
https://aimcd.net/

Visit Our Clinical Resource Center at
ExchangeCME.com/SMBRIDGEResources

EXCHANGE CME™

INTEGRITAS COMMUNICATIONS

Routine Monitoring of Patients With Nonadvanced SM

Every 6-12 months
depending on symptom presentation and burden

- ❍ Serum tryptase level
- ❍ *KIT* D816V VAF
- ❍ CBC/Diff
- ❍ CMP
- ❍ Physical examination, including skin/lesions
- ❍ QoL/Symptom burden
- ❍ DEXA scan every 1-3 years
- ❍ Abdominal sonography (if palpable hepatosplenomegaly)
- ❍ Repeat BM biopsy is only necessary with clinical or laboratory changes

DEXA, dual-energy X-ray absorptiometry.

If laboratory results or symptoms change, therapeutic adjustment <u>should</u> be considered.

Common Triggers for Patients With SM

TRIGGERS	EXAMPLES
Venoms	Bee, wasp, mixed vespids, fire ants
Food & Beverages	Alcohol consumption
Allergens	Pollen, pet dander, dust mites
Medications	Opioids, some antibiotics, NSAIDs, contrast dyes
Acute infection	Viral, bacterial, fungal
Pain	Emotional, physical
Environment	Heat, cold, sudden changes in temperature, natural and chemical odors, sun/sunlight
Fatigue	Lack of sleep/sleep deprivation
Physical triggers	Mechanical irritation, friction, vibration, exercise
Surgery	Anesthesia
Procedures	Colonoscopy, endoscopy, interventional radiology
Vaccinations	

NSAID, nonsteroidal anti-inflammatory drug.

Nonadvanced Systemic Mastocytosis (SM):

A Clinician's Reference Pocket Guide

Nonadvanced SM Subtypes

- Indolent SM (ISM, most common)
- Bone marrow mastocytosis (BMM)
- Smoldering SM (SSM, highest risk of progression)

Clinical Suspicion Cues

- ❍ Pigmented cutaneous lesions that urticate with pressure (Darier's sign positive)
- ❍ Anaphylaxis to insect venom
- ❍ History of anaphylaxis, especially if associated with baseline or event-related tryptase increases
- ❍ BST >8 ng/mL
- ❍ History of fractures (especially vertebral)
- ❍ History of hypotensive episodes resulting in presyncope or syncope + absence of urticaria and angioedema + elevated BST level
- ❍ History of flushing, itching, or hives
- ❍ History of unexplained abdominal pain or other GI symptoms
- ❍ History of fatigue, brain fog, or headaches
- ❍ Symptoms triggered by temperature changes, friction, stress, alcohol, or medications

BST, basal serum tryptase; GI, gastrointestinal.

BRIDGE^{SM} BUILDING BRIDGES

BETWEEN TREATMENT CENTERS & COMMUNITY PRACTICES: REDUCING KNOWLEDGE GAPS IN MANAGEMENT OF SYSTEMIC MASTOCYTOSIS

WHO 2022 SM Diagnostic Criteria

MAJOR CRITERIA	MINOR CRITERIA
Multifocal dense infiltrates of MCs (≥15 MC in aggregates) detected in BM and/or ECO(s).	>25% of all MCs with atypical MC morphology on BM smears or in other ECO(s)
1 major criterion + 1 minor criterion OR ≥3 minor criteria	*KIT* D816V or other activating *KIT* mutation detected
	Baseline serum tryptase >20 ng/mL; in the case of known HαT, adjust tryptase level
	CD2, CD25, and/or CD30 on MCs

In the case of HαT, the expected level of tryptase can be calculated via

$$\frac{\text{BST}}{1 + \text{extra copy numbers of } \textit{TPSAB1}}$$

BM, bone marrow; BST, basal serum tryptase; ECO, extracutaneous organ; HαT, hereditary alpha tryptasemia; MC, mast cell; *TPSAB1*, tryptase alpha/beta 1; WHO, World Health Organization.

NCCN Guidelines: Symptom-Directed Treatment Strategies

Organ Involvement/ Symptom	Additional Treatments
Skin: pruritus, flushing, urticaria, angioedema dermatographism[a]	1. H_1 and H_2 blockers 2. Leukotriene receptor antagonist 3. Aspirin 4. Ketotifen 5. Cromolyn sodium, topical
GI: abdominal pain, cramping, diarrhea, GERD/heartburn, nausea, vomiting	1. H_2 blockers 2. Cromolyn sodium 3. Proton pump inhibitor 4. Leukotriene receptor antagonist 5. Ketotifen
Hypotensive episodes/ anaphylaxis	• Epinephrine IM (acutely), supine positioning
Cardiovascular/pulmonary: presyncope, tachycardia, wheezing, throat swelling	1. H_1 and H_2 blockers 2. Corticosteroids 3. Omalizumab
Osteopenia/osteoporosis	• Supplemental calcium and vitamin D, bisphosphonate; BMD assessment
Neurologic: headache, cognitive impairment (eg, brain fog, poor concentration and memory), depression	1. H_1 and H_2 blockers 2. Cromolyn sodium 3. Aspirin 4. Ketotifen

BMD, bone mineral density; GERD, gastroesophageal reflux disease; H, histamine; IM, intramuscular; NCCN, National Comprehensive Cancer Network; QoL, quality of life; R, receptor.

[a]Psoralen and ultraviolet A (PUVA) therapy can improve cutaneous manifestations of SM, in some cases resulting in disappearance of skin lesions; however, lesions recur with cessation of treatment.

NCCN. 2025. https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf

Most Commonly Used Antihistamines for Patients With Nonadvanced SM

ANTIHISTAMINE CLASS	MOST COMMONLY USED FOR SM SYMPTOMS
H_1R Blockers (1st generation)	Diphenhydramine, hydroxyzine
H_1R Blockers (2nd generation)	Cetirizine, fexofenadine, levocetirizine
H_2R Blockers	Famotidine

Avapritinib is FDA-approved for adults with ISM.

Consider adding avapritinib when optimized symptomatic treatment regimens are not adequately mitigating QoL and symptom burdens.

FDA, United States Food and Drug Administration.

For Patients With ISM: Adding Avapritinib

- Dosing: 25 mg QD on an empty stomach
- Avoid coadministration with strong and moderate CYP3A inhibitors and inducers
- Not recommended for the treatment of patients with ISM with platelet counts of less than 50 x 10^9/L

Avapritinib Monitoring Suggested Best Practice

Bloodwork (CMP, CBC/Diff) and physical assessment at **3 and 6 months after** starting avapritinib, then **every 6-12 months** depending on symptom presentation and burden.

CBC/Diff, complete blood count with differential; CMP, comprehensive metabolic panel; CYP, cytochrome P450; QD, once daily.

Drugs@FDA. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/212608s013lbl.pdf