DISCOVERSM

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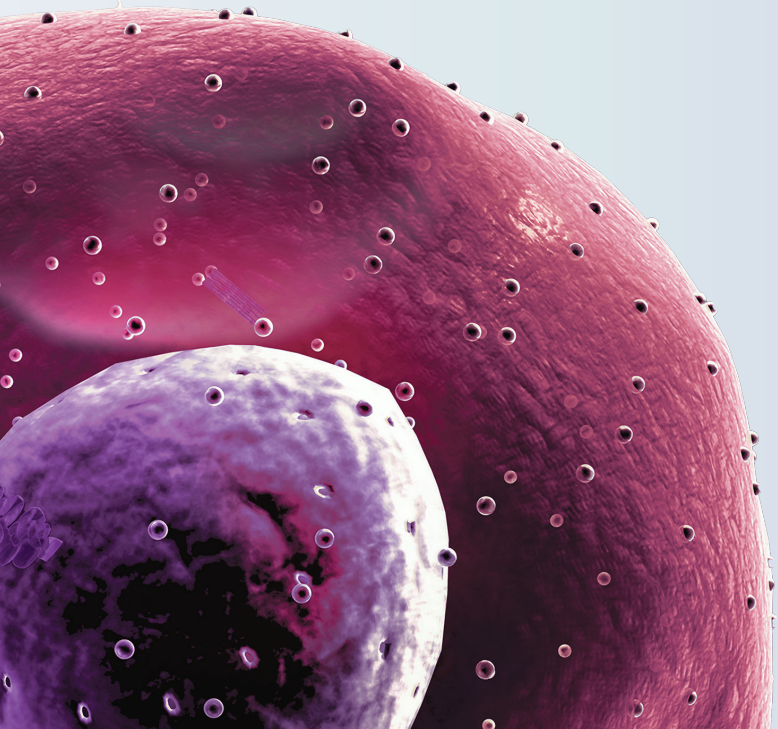
# DIAGNOSING SYSTEMIC MASTOCYTOSIS

## THE INTEGRAL ROLE OF A PATHOLOGIST

**The complexity of a systemic mastocytosis (SM) diagnosis calls for a thorough and specific analysis by a haematopathologist[1,2]**



## Histopathology

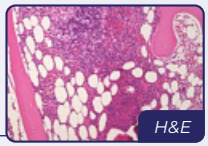
# The criteria for diagnosing SM primarily require histopathological investigation of a bone marrow biopsy/bone marrow aspirate.[2,3]

Evaluation of both the **major** and **minor** diagnostic criteria is instrumental in the diagnosis of SM.[2]

SM-specific immunohistology is key in assessing several of the diagnostic criteria. Immunohistochemical stains against **CD117,[3] tryptase, CD25 and/or CD2** are commonly used, and staining for **CD30** may also be performed.[2]

### Major criterion

**Multifocal dense infiltrates of mast cells (≥15 mast cells in aggregates)** in bone marrow biopsies and/or in sections of other extracutaneous organ(s)




Bone marrow findings can be subtle/sparse in routine H&E stains, and classic aggregates can be absent in a fraction of cases

**Ordering a panel of immunohistochemical stains is useful for a complete diagnostic work-up**

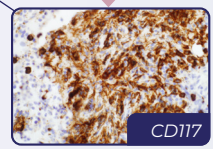
### Minor criteria

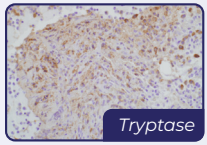
**≥25% of all mast cells are atypical cells (type I or type II) on bone marrow smears or are spindle-shaped in mast cell infiltrates.** Detected in sections of bone marrow or other extracutaneous organs

Activating *KIT* point mutation(s) at codon 816 or in other critical regions of *KIT*. In bone marrow or another extracutaneous organ

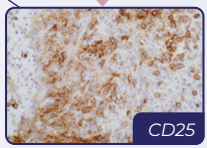
Mast cells in bone marrow, blood or another extracutaneous organ express one or more of CD2 and/or CD25 and/or CD30

Baseline serum tryptase concentration >20 ng/mL (in the absence of an unrelated myeloid neoplasm; it does not count as a minor criterion for SM when an associated haematologic neoplasm is present). In the case of a known hereditary alpha tryptasaemia (HαT), the tryptase level should be adjusted.




The most specific markers of mast cells




Aberrant expression

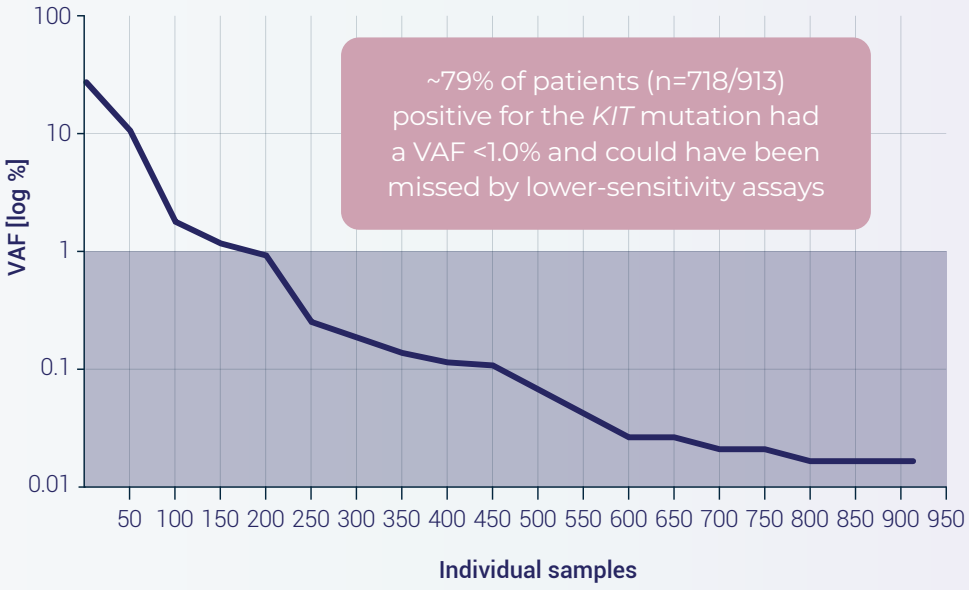
Images courtesy of Professor George, University of Utah School of Medicine.

CD=cluster of differentiation; H&E=haematoxylin and eosin; *KIT*=*KIT* proto-oncogene, receptor tyrosine kinase; SM=systemic mastocytosis.

# Guidelines recommend high-sensitivity *KIT* D816V assays when SM is suspected.[2,4]

- The *KIT* D816V mutation is the main driver of SM in ~95% of cases.[5–7]
- Low-sensitivity tests can lead to false-negative results.[4]
- Consider ordering a high-sensitivity *KIT* D816V test when you order serum tryptase.[2,4]

## Labcorp data: VAF of 913 consecutive patients positive for *KIT* D816V[8]*




*All testing was performed by Laboratory Corporation of America between October 2021 and April 2025.

*KIT=KIT* proto-oncogene, receptor tyrosine kinase; SM=systemic mastocytosis; VAF=variant allele frequency.

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**The criteria for diagnosing SM primarily require histopathological investigation of a bone marrow biopsy/bone marrow aspirate.[2]**

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**SM may still be present despite a serum tryptase level ≤20 ng/mL and undetectable *KIT* D816V mutation[2]**

**References: 1.** Rets AV, George TI. *Am J Clin Pathol.* 2024;162(4):332–348. **2.** Valent P, *et al. Hemasphere.* 2021;5(11):e646. **3.** WHO Classification of Tumours Editorial Board. Haematolymphoid tumours [Internet]. Lyon (France): International Agency for Research on Cancer. Available at: https://tumourclassification.iarc.who. int/chapters/63. Accessed February 2026. **4.** Hoermann G, *et al. J Allergy Clin Immunol Pract.* 2022;10(8):1953–1963. **5.** Ungerstedt J, *et al. Cancers (Basel).* 2022;14(16):3942. **6.** Kristensen T, *et al. J Mol Diagn.* 2011;13(2):180–188. **7.** Garcia-Montero AC, *et al. Blood.* 2006;108(7):2366–2372. **8.** Data on file. Blueprint Medicines Corporation, Cambridge, MA. 2025.

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