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# Integrating a Rare Disease into Practice: Development of a Toolkit for Systemic Mastocytosis

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Authors' disclosures of conflicts of interest are found at the end of this article.

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**Abstract**

Systemic mastocytosis (SM) exemplifies the diagnostic and management challenges associated with rare diseases, which often involve prolonged time to diagnosis, limited access to clinical experts, and persistent symptom burden. Advanced practitioners (APs) are increasingly responsible for the care of patients with rare and classical hematologic disorders. The Advanced Practitioner Society for Hematology and Oncology (APSHO) convened a multidisciplinary, AP-led steering committee to evaluate the AP role in managing SM, develop an online toolkit, and design surveys to identify best practices, unmet needs, and practical strategies for improving care for patients living with indolent systemic mastocytosis (ISM). The toolkit emphasizes early symptom recognition, integration of validated patient-reported outcome measures, and incorporation of disease-specific tools into clinical workflows and electronic medical records (EMRs). The emergence of targeted therapies, such as avapritinib for both advanced and indolent SM, has further highlighted the need for AP education on novel disease mechanisms and treatment strategies. This project demonstrates a replicable model for developing educational and clinical resources to support APs in managing rare diseases and improving patient-centered care.

Rare diseases pose numerous challenges for patients, clinicians, and researchers, including difficulties in establishing a diagnosis, limited clinical trial accrual, and barriers to access to clinical experts (DeSantis et al., 2017). Classical hematology and rare diseases continue to be underserved across practice settings with limited training for fellows and advanced practitioners (APs; Panwar et al., 2023; West et al., 2024). Limited exposure to patients with rare diseases may deter effective differential diagnosis and

clinical management of patients living with rare diseases and classical hematology diagnoses.

Patients with rare diseases, including systemic mastocytosis (SM), see an average of 7.3 providers across multiple specialties before receiving an accurate diagnosis (Jennings et al., 2018). The median time from symptom onset to diagnosis of SM is 3 years but may take as long as 9 years (Jennings et al., 2018). Patients with SM take an average of 3 to 11 over-the-counter medications and as many as 5 prescription medications to manage their SM (Pulfer et al., 2021). Over-the-counter medications are not covered by insurance. Symptom burden is the leading driver for SM patients to seek medical care (Zeiger et al., 2025). The challenges in reaching a diagnosis together with the cadre of providers across multiple specialties involved with symptomatic patients present barriers in making a timely diagnosis of SM.

## BUILDING AN AP-CENTRIC MULTIDISCIPLINARY TOOLKIT FOR SYSTEMIC MASTOCYTOSIS

Recognizing the challenge most hematology/oncology APs face in managing a broad range of diagnoses and the growing AP role in classical hematology, the Advanced Practitioner Society for Hematology and Oncology (APSHO) convened an AP-led multidisciplinary steering committee to: 1) evaluate the role of APs in the diagnosis, management, and support of patients living with rare diseases using indolent systemic mastocytosis (ISM) as a model, 2) develop an online AP toolkit for SM for all subtypes as a model for improving AP knowledge and skills for managing rare diseases, and 3) launch a multidisciplinary AP and ISM patient survey to evaluate AP and ISM patient experiences, including evaluation and management of symptom burden. The APSHO Quality Improvement Toolkit (available to APSHO members at https://www.apsho.org/research-and-quality-improvement; Kurtin et al., 2023) provided the foundation for engaging APs, patients, advocacy organizations, and physician colleagues with expertise in SM to elucidate best practices and identify unmet needs (Tables 1 and 2).

Advanced practitioners play a critical role in managing rare diseases through identification and management of symptoms and clinical findings across multiple diseases. Making a diagnosis of SM requires considering potential etiologies, connecting symptoms that are common to SM, and integrating this into the process of differential diagnosis. Familiarity with the symptom profile of SM, including triggers, will improve the AP approach to connecting those symptoms to a possible diagnosis of SM and implementation of strategies for managing the symptoms and the disease.

Systemic mastocytosis is a lifelong disease for most patients. The unpredictable and at times life-threatening constellation of symptoms characteristic of SM, the difficulty in reaching a diagnosis, limited treatment options, and a paucity of clinical expertise create challenges for patients and caregivers. Although there has been progress in understanding the pathobiology of SM and drivers of symptoms associated with mast cell mediators, most patients continue to report a significant symptom burden that interferes with their quality of life despite taking multiple symptom-directed therapies. Patients living with SM, whether diagnosed or not, often minimize the impact or severity of symptoms when discussing symptoms with clinicians because they are accustomed to living with poorly controlled symptoms (Jennings et al., 2018).

Until recently, treatments for SM were limited to agents directed at mast cell mediators, offering temporary and often limited benefit in reducing symptom burden. With the discovery of the *KIT* D816V mutation as the primary driver mutation of SM and SM-associated symptoms, clinical trials using agents to target this mutation are underway with the US Food and Drug Administration (FDA) approval of avapritinib (Ayvakit), a first-in-class selective *KIT* D816V inhibitor in April 2021 for advanced SM and in May 2023 for ISM. Integrating novel therapies into practice for rare diseases requires focused and comprehensive education for disease state, pathways, targets, and patient factors (Kurtin, 2017).

Symptom burden is a subjective concept that relies on patient self-report and clinician interpretation. Eliciting symptoms from patients with long-standing symptoms that have not been connected to any specific diagnosis requires patient-centered communication. Quantifying the

**Table 1. Development of the APSHO Toolkit for Systemic Mastocytosis Using the APSHO Quality Improvement Toolkit Model**

| Elements of the APSHO QI Toolkit | Development of APSHO Toolkit for SM |
|---|---|
| • Establish a steering committee or QI project teams<br>• Include representatives from all key stakeholders and obtain buy-in | • Establish AP project lead and APSHO/Conexiant project team. Hold weekly meetings<br>• Recruit steering committee members: heme/onc and allergy and immunology APs, physician specialists in SM, SM patient, SM advocacy representative<br>• Conduct a series of meetings (group and individual) with the project lead and steering committee |
| • Agree on method from analysis to implementation and evaluation<br>• Identify essential steps of process improvement | • Gain input from key stakeholders: heme/onc APs, allergy and immunology APs, physician experts, SM patient, SM advocacy representative, and multidisciplinary SM focus group<br>• Integrate feedback into toolkit and survey development<br>• Obtain feedback from stakeholders throughout process |
| • Define the problem or opportunity<br>• Define the aims or outcomes<br>• Define a manageable scope and timeline<br>• Define measurable outcomes, including sources of data | • Rare diseases, including SM, are underrepresented in AP education and training<br>• Goals: (1) Evaluate the role of APs in the diagnosis, management, and support of patients living with rare diseases using SM as a model; (2) develop an online AP toolkit for SM as a model for improving AP knowledge and skills for managing rare diseases; and (3) launch an multidisciplinary AP and SM patient survey to evaluate AP and SM patient experiences with SM, including evaluation and management of symptom burden<br>• Project timeline: September 2024–March 2025<br>• Outcomes: Toolkit for SM, AP and patient survey, publications, and posters |
| • Perform program analysis | • Program analysis: JADPRO Insight Forum Panel Discussion (September 2024); JADPRO Live SM Focus Group (November 2024); JADPRO Live Rare Disease Reception (November 2024) were used to solicit input and collect data from APs, physicians, patients, and advocacy organizations to guide the Toolkit for SM and survey development. |
| • Address organizational compliance<br>• Project development does not require IRB approval | • Project identified as a priority initiative by APSHO and Conexiant<br>• Project development does not require IRB approval<br>• Patient and AP survey are HIPA compliant, voluntary and exploratory in nature |
| • Plan for implementation/present findings<br>• Define next steps to build on your success and overcome continued barriers outcomes | • Toolkit for SM launched April 2025<br>• Practice matters article submitted for publication to JADPRO (online first) March 2025<br>• Research and scholarship paper submitted for publication to JADPRO (online first) March 2025<br>• Poster to be submitted for JADPRO Live 2025 highlighting project and next steps |

*Note.* APSHO = Advanced Practitioner Society for Hematology and Oncology; AP = advanced practitioner; SM = systemic mastocytosis; QI = quality improvement; heme/onc = hematology/oncology; HIPAA = Health Insurance Portability and Accountability Act; IRB = institutional review board; JADPRO = Journal of the Advanced Practitioner in Oncology.

**Table 2. Timeline for Development of the APSHO AP Toolkit for Systemic Mastocytosis**

*September to October 2024*

- ISM Steering Committee
  a. Chair: Sandra Kurtin, PhD, ANP-BC, FAPO (Hematology AP)
  b. Susan Woodward, MSN, APRN, AOCNP (Hematology AP)
  c. Shonna Snyder, PhD (Patient Advocacy Research)
  d. Erin Kolb, MSN, FNP-C (Allergy and Immunology AP)
  e. Shawna Hull (Patient Advocate Representative)
- ISM survey development
- ISM panel discussion at *JADPRO* Insight Forum

*November to December 2024*

- ISM survey development continued
- ISM panel discussion Q&A session
- ISM patient and AP surveys launch
- SM Steering Committee
  a. Sandra Kurtin, PhD, ANP-BC, FAPO, Chair
  b. Cem Akin, MD, PhD (Allergy and Immunology Physician)
  c. Tracy I. George, MD (Pathologist)
  d. Edward Pearson, MD (Hematologist)
- SM steering committee meetings
- SM steering committee creates first iteration of Toolkit for SM
- SM focus group at JADPRO Live
  a. Moderator: Sandra Kurtin, PhD, ANP-BC, FAPO
  b. Steering Committee: Tracy I. George, MD, and Edward Pearson, MD
  c. Focus group members: Charise Frandsen, MPAS, PA-C (Allergy and Immunology AP), Erin Kolb, MSN, FNP-C (Allergy and Immunology AP), Susan Woodward, MSN, APRN, AOCNP (Hematology AP), Nichole Lee, AG-ACNP, MSN (Heme/onc AP), Haley Goulson, PA-C (Heme/onc AP), Kimberly Smith, AGNP-C (Heme/onc AP), and Shreya Jain, PA-C (Heme/onc AP)

*January to February 2025*

- ISM surveys collect data until February 2025
- Design begins for Toolkit for SM

*March to April 2025*

- Manuscript development and submission
- Launch of Toolkit for SM (https://www.apsho.org/apsho-aptoolkit-sm)

patient's experience is an elusive target fraught with the nuances of patient-reported outcomes. This requires clinicians to evaluate changes in symptoms over time to effectively identify potential interventions and then evaluate the effectiveness of those interventions. Quality of life is frequently impaired in patients with SM and should be assessed in all patients by using validated disease-specific tools (e.g., Mastocytosis Quality of Life Questionnaire [MC-QoL], Mastocytosis Quality of Life Questionnaire [MQLQ], or Quality of Life in Mastocytosis Scale [QLMS]).

The challenge of effective communication across clinicians and over time requires integrating validated tools into clinicians' workflows within a patient visit and within the electronic medical record (EMR). Validated tools used in clinical trials are rarely embedded in the EMR. Trends over time are difficult to discern unless vigilant clinicians incorporate this information into progress notes or embedded tools such that it is visible across team members and specialties. Unfortunately, barriers remain in actualizing this workflow, limiting the application of these validated tools into mainstream clinical practice. Identifying clinical and informatic champions within each practice to create EMR solutions will be required to overcome these barriers.

Engagement of clinicians across multiple specialties promotes an awareness of practice patterns and workflows that facilitate improved cross-specialty communication and collaboration. Building a network across these specialties and clinicians will enhance continued collaborations. Including patients and advocacy organizations is essential to fully understanding the patient experience and developing tools that adequately reflect the lived experience of SM and

other rare diseases. The culmination of the project resulted in deployment of the Toolkit for SM (https://www.apsho.org/apsho-aptoolkit-sm) and ISM patient and AP surveys. Application of the APSHO Quality Improvement Toolkit and lessons learned from activities used to develop the Toolkit for SM may be applied to developing similar programs for other rare cancers. ●

## Disclosures

Dr. Kurtin has served as a consultant for Agios, Blueprint Medicines, and GSK, and received honoraria from Agios and GSK. Dr. Akin has served as a consultant for Novartis and has served as a consultant or received research grants from Blueprint Medicines, Cogent Biosciences, and Telios. Dr. George has served as a consultant for Beckman Coulter, Blueprint Medicines, Cogent Biosciences, and Incyte. Dr. Pearson, MD, has served as a consultant or speaker for AbbVie/Genmab, Adaptive Biotechnologies, ADC Therapeutics, AstraZeneca, Blueprint Medicines, Bristol Myers Squibb, Celgene, Genentech, GlaxoSmithKline, Incyte Corporation, Lilly USA, PharmaEssentia, Rigel Pharmaceuticals, and Sanofi.

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