Transcript Details
This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/living-with-systemic-mastocytosis-bridging-clinical-decisions-and-patient-realities/54389/

Released: 04/24/2026
Valid until: 04/24/2027
Time needed to complete: 15 Minutes

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Living With Systemic Mastocytosis: Bridging Clinical Decisions and Patient Realities

Announcer:
Welcome to CE on ReachMD. This activity, titled “Living With Systemic Mastocytosis: Bridging Clinical Decisions and Patient Realities” is provided by TotalCME.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Akin:
Hello. I'm Dr. Cem Akin from the University of Michigan, and I'd like to welcome you to our patient-clinician connection on systemic mastocytosis.

Systemic mastocytosis is a rare and often misunderstood hematologic disorder characterized by clonal mast cell proliferation and activation, resulting in a wide spectrum of symptoms that can affect nearly every organ system. Patients may experience cutaneous manifestations, gastrointestinal distress, neurologic symptoms, and in some cases life-threatening anaphylaxis.

For many patients, the diagnostic journey is prolonged and frustrating. Symptoms are often nonspecific and underestimated, leading to delays in diagnosis and misattribution to other conditions.

Today, we will explore how to recognize and diagnose systemic mastocytosis, review current evidence-based treatment approaches, and discuss how to integrate patient perspectives into shared decision-making and long-term management. I'll illustrate these concepts through patient interviews and educational vignettes to highlight how we can bridge clinical decision-making and real-world patient experience. So let's begin.

Dr. Akin:
Hi, Porscha, can you tell me about your medical journey from the initial onset of your symptoms to your actual diagnosis of indolent systemic mastocytosis?

Porscha:
Absolutely. Yeah. So it started over 15 years ago. I was having allergies, sensitive to soaps, detergents, air fresheners, and I would have rashes on my hands and my face, was flushing a lot, and had constipation and diarrhea, acid reflux, and no one was really putting that together as a mast cell problem. It's just an allergy problem. I went to see gastroenterologists. They said I had IBS and GERD. And dermatologists, it was eczema and a little bit of psoriasis. Went to a neurologist, and I went to pulmonology, and they said, ‘Okay, so this is just asthma exacerbations.’

And my allergist at the time had done fellowship at Cleveland Clinic, and she said, ‘Well, I think it has to do with mast cells. So I really

want to check out your tryptase,' because everything was kind of escalating. And tryptase came back high. Not very surprised about that. So she actually left the practice, and I was lucky enough to have somebody come in to take over who was familiar with mast cell disorders, and I was having hives, hives all over and having gastritis. And he wanted to test me for the KIT mutation when I started having bowel obstructions and the KIT mutation was positive, and he referred me over to heme-onc.

My bone marrow was actually negative first time, but I developed like hives and all of my old scars, and over the course of the last year—this was recently for me actually, so it was like 24-25, my immune system started to malfunction, and I was having pneumonia all the time. And went back to the heme-onc. Had a biopsy of my—as I was having more digestive symptoms. Biopsy was positive for the mast cells this time.

Dr. Akin:
Systemic mastocytosis, or SM, presents with heterogeneous manifestations.

Diagnosis requires meeting WHO criteria. The major criterion is bone marrow or other extracutaneous tissue biopsies, such as gastrointestinal biopsies, showing dense mast cell infiltrates. And according to WHO, you need one major and one of these following minor criteria. If the major criterion is absent, you need to have three of these minor criteria to meet the diagnosis.

The first one is presence of KIT D816V mutation. The second is elevated serum tryptase level. The third minor criterion is abnormal mast cell morphology. And the fourth criterion is abnormal mast cell markers such as CD25, CD2, or CD30.

Once we make the diagnosis, it is critical to distinguish among non-advanced and advanced variants.

Non-advanced systemic mastocytosis constitutes the majority of the patients. Many of these patients are highly symptomatic, but they are expected to have a similar life expectancy to general population.

Among non-advanced SM, the most common subgroup is indolent systemic mastocytosis. And then there are other groups called bone marrow mastocytosis and smoldering systemic mastocytosis.

Which brings us to the advanced systemic mastocytosis. So these are patients either presenting with another myeloid disorder such as myeloproliferative or myelodysplastic syndrome, or they experience complications due to the high degree of mast cell infiltration into bone marrow or other tissues interfering with the functioning of the tissue.

Accurate diagnosis and subtyping inform prognosis and treatment selection. Early referral to specialists experienced in mast cell disorders can shorten these diagnostic delays and improve patient outcomes.

Let's return to our conversation with Porscha after diagnosis is confirmed.

Dr. Akin:
What medications did you initially take after the diagnosis of indolent systemic mastocytosis was made?

Porscha:
So I took cetirizine, famotidine, diphenhydramine, I took quercetin and omalizumab, cromolyn. It just was not handling the symptoms that I was having that were escalating.

Dr. Akin:
Symptom management of indolent systemic mastocytosis includes first-line therapies, traditionally in the group of anti-mediator treatments. So these include H1 antihistamines or H2 antihistamines, antileukotriene medications, cromolyn sodium as a mast cell stabilizer, and in some patients we use omalizumab or glucocorticoids, especially if they present with recurrent anaphylaxis.

While helpful, these therapies may not always adequately control symptom burden or disease activity and may have side effects. This brings us to the targeted therapy approach. The discovery of KIT D816V as a driver mutation in most cases of systemic mastocytosis has led to the development of targeted therapies such as KIT inhibitors or tyrosine kinase inhibitors. And in this disease, avapritinib is currently the only approved tyrosine kinase inhibitor for indolent systemic mastocytosis.

And in advanced systemic mastocytosis, we have avapritinib as well as another kinase inhibitor called midostaurin that are currently approved for advanced systemic mastocytosis.

Let's review some evidence from pivotal trials starting with advanced systemic mastocytosis. The efficacy of midostaurin was first established in a phase 2 trial. And midostaurin became the first tyrosine kinase inhibitor to be approved for advanced systemic mastocytosis with KIT D816V mutation. And the trial produced some modest results.

Then we tested avapritinib in EXPLORER and PATHFINDER trials. And in these trials, the drug had about 75% overall response rate, much improved over midostaurin, and about 20-30% of these responses were complete remissions.

In these trials, one of the complications, or the side effects of the medication, was intracranial hemorrhages, especially in patients with platelet counts less than 50,000 and they received the drug at higher doses, on an average of 200 mg daily dose.

Another side effect that was encountered at high doses was cognitive dysfunction. And neither of these side effects were seen in indolent systemic mastocytosis trial, which is the PIONEER trial.

So PIONEER trial compared the efficacy of 25 mg to that of placebo. And at the end of 24 weeks, the primary endpoint was symptom improvement, and that was significantly improved in patients on avapritinib as compared to placebo.

In terms of the adverse events, the drug was well tolerated, and the most commonly encountered adverse event was edema.

Dr. Akin:
Okay. So it sounds like you were on multiple anti-mediator type medications with H1 antihistamines, H2 antihistamines, and mast cell stabilizers, including cromolyn, and even omalizumab. And these did not seem to control your symptoms properly. And what medication did you get when these therapies failed?

Porscha:
I did go on the avapritinib. They told me about the efficacy for patients who went through the trial. There was a handout. My allergist actually was cooperating with my heme-onc and gave me the information that explained how this had improved the symptoms of other patients who have the same kind of issues that I have had, like bone pain and nausea and the anaphylactic reactions and digestive symptom reactions, the things like diarrhea and so on.

Dr. Akin:
In advanced SM, cognitive effects were among the most clinically relevant adverse events associated with avapritinib and require early recognition and patient counseling. Grade 1 being mild, in which avapritinib is continued or withheld until improvement to baseline or the symptom completely resolves. Grade 2 to 3 are moderate to severe events, and for these patients, withholding avapritinib is recommended until improvement to baseline or to grade 1 level or resolution. And finally, grade 4 is a life-threatening adverse event where the medication should be permanently discontinued.

For other adverse events like cytopenias and gastrointestinal toxicities, appropriate monitoring and early intervention are essential to optimize treatment adherence and patient outcomes. These adverse events are not encountered frequently in indolent systemic mastocytosis.

Let's continue our conversation with Porscha after she has been on avapritinib for about 3 months.

Dr. Akin:
Okay, so can you tell us a little bit more about your experience with avapritinib so far?

Porscha:
Yes, actually, tryptase levels have gone down. So it did decrease my nausea. It helped with the motility, which was a surprise for me, with the digestive issues that I have been having. Overall, it has been positive.

Dr. Akin:
Shared decision-making in systemic mastocytosis requires the patient perspective, and also discussing patient adherence and persistence, because these medications are actually great advancements in reducing the symptoms and modifying the underlying disease, but nevertheless they need to be taken consistently.

In terms of the optimal mastocytosis management strategies, multidisciplinary care is often very important, because no single specialist will have the clinical knowledge to take care of all these organ manifestations. And this often involves a hematologist, an allergist, a gastroenterologist, a dermatologist, in some cases an endocrinologist to manage the bone symptoms or osteoporosis which is a common comorbidity.

In closing, systemic mastocytosis presents complex clinical challenges but also profound opportunities to improve patient lives through evidence-based personalized care. By recognizing the multi-system burden of disease, applying targeted therapies appropriately, and integrating patient experience into shared decision-making, we can connect clinical decisions with patient realities.

Thank you for joining me for this patient clinician connection on living with systemic mastocytosis. Goodbye.

Announcer:
You have been listening to CE on ReachMD. This activity is provided by TotalCME.

To receive your free CE credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.