Disease Progression in Patients with Systemic Mastocytosis: A US Population-Level Analysis Using Health Claims-Based Dataset

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Background

- Systemic mastocytosis (SM) is a rare disease driven by the KIT D816V mutation in ~95% of patients[1,2]
- ~95% of patients with SM have non-advanced stages of disease (indolent SM [ISM] and smoldering SM), and the standard of care is focused on symptom management[3]
- While World Health Organization (WHO) criteria differentiate between subtypes of mastocytosis, there remains a lack of understanding of patterns of disease progression between and worsening within SM subtypes[4,5]
- Comprehensive testing and specialist care management is needed to ensure accurate diagnosis and treatment of patients with SM

Objectives

- To develop a novel claims-based algorithm to identify SM cases and assess disease progression and worsening
- To describe SM treatment utilization and unmet treatment need in the era of KIT inhibitors

Analysis Design

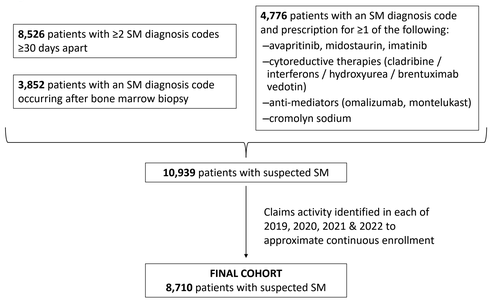
Cohort Identification

- This analysis utilized a large nationally representative United Stated (US) claims database including patients with commercial, Managed Medicaid, and Medicare Advantage coverage, 2015-2022. Patients were included if they had claims in each year 2019-2021, pragmatically approximating continuous enrollment
- A novel claims-based algorithm based on WHO diagnostic criteria (2016)[5] was developed
- Patients were selected if they fulfilled ≥1 of the following criteria (Figure 1):
  - ≥2 diagnoses with an SM-specific International Classification of Diseases, 10th Revision (ICD-10) code (D47.02, C96.21, C94.3X) ≥30 days apart in any setting of care
  - Bone marrow biopsy followed by 1 SM diagnosis claim code in any setting of care;
  - 1 SM diagnosis code in any setting of care and ≥1 prescription claim for an SM-specific treatment (avapritinib, midostaurin, imatinib, cladribine, interferons, hydroxyurea, brentuximab vedotin, omalizumab, montelukast, or cromolyn sodium)
- Qualifying patients stratified by SM subtype: advanced SM, higher symptom-burden ISM, or lower symptom-burden ISM (Figure 2)

Outcomes

- Treatment rates of select SM-directed therapies during 2021
- Disease progression

Figure 1. Patient Cohort Identification



Results

- 8,710 patients with SM qualified for analysis (Figure 1), including 1,587 advanced SM, 2,705 ISM-higher, and 4,415 ISM-lower patients (Table 1)
- Mean age at diagnosis was 49 years
- Racial breakdown strongly biased towards whites (85.7% of all SM) but may reflect inequities regarding access to healthcare rather than true underlying epidemiologic differences
- Female predominance (69.8% of all SM) aligns with findings from other claims-based studies[6]
- A majority of patients were enrolled in commercial insurance plans (67.2% of all SM)

Figure 2. SM Subtype Definitions

Advanced SM
≥2 Mast cell leukemia (MCL) diagnosis code (C94.3X)
OR
≥2 Aggressive SM diagnosis code (C96.21)
OR
≥1 MCL/Aggressive SM diagnosis code (C94.3x, C96.21) occurring following an ambiguous mast-cell diagnosis code*
OR
≥1 SM codes (C94.3x, C96.21, D47.02) in addition to ≥1 associated hematologic neoplasm (AHN) code (in order to capture SM-AHN patients)

Higher symptom-burden ISM
≥2 SM (D47.02)
OR
SM diagnosis code (D47.02) occurring following an ambiguous mast cell neoplasm diagnosis code*
AND
Any of the following:
- ≥2 diagnosis codes indicative of C-finding
- ≥2 prescriptions for advanced SM-directed therapies (tyrosine kinase inhibitors [TKIs], cytoreductive therapies incl. interferons / cladribine / brentuximab vedotin, omalizumab)
- ≥1 diagnosis code indicating compromised bone, hepatomegaly, splenomegaly or weight loss
- High frequency anaphylaxis/epinephrine injector (≥4 claims)

Lower symptom-burden ISM
All remaining patients in cohort

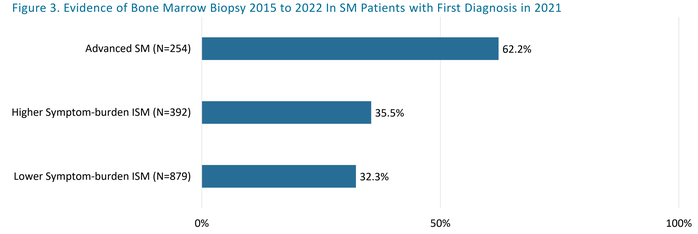
***D47.09** Other mast cell neoplasms of uncertain behavior, **C96.20** Malignant mast cell neoplasm, unspecified, **C96.22** Mast cell sarcoma, **C96.29** Other malignant mast cell neoplasms

Table 1. Baseline Patient Demographics, in 2021

Parameter	All SM (2021)	Advanced SM (2021)	Higher Symptom-burden ISM (2021)	Lower Symptom-burden ISM (2021)
Number of Unique Patients	8,710	1,587	2,706	4,417
Age at first SM diagnosis Mean (standard deviation)	49.3 (18.4)	55.1 (17.4)	47.5 (16.9)	48.4 (19.2)
Age at end of 2021 (%)				
<18	4.9%	2.0%	3.5%	6.7%
18 – 39	20.5%	13.8%	23.8%	20.9%
40 – 54	27.3%	24.4%	30.0%	26.6%
55 – 65	23.3%	23.6%	23.8%	22.8%
>65	24.1%	36.2%	18.9%	23.0%
% Male	30.2%	38.5%	25.1%	30.4%
Race / Ethnicity (%)				
Unknown	45.8%	40.9%	44.3%	48.5%
Among known:				
White	85.7%	82.5%	87.3%	85.9%
Hispanic or Latino	5.4%	7.2%	5.0%	4.9%
Black/African American	3.7%	5.0%	3.6%	3.3%
All Other	5.1%	5.3%	4.0%	5.9%
Region (%)				
Northeast	19.6%	17.5%	21.1%	19.5%
South	32.6%	34.3%	31.3%	32.7%
Midwest	21.7%	21.6%	22.9%	20.9%
West	21.4%	21.7%	20.0%	22.1%
Unknown	4.8%	4.9%	4.8%	4.7%
Payer (%)				
Commercial	67.2%	58.5%	69.2%	69.0%
Medicare Advantage	6.8%	6.0%	7.4%	6.6%
Medicaid	22.7%	32.0%	20.1%	21.0%
Other or Unknown	3.3%	3.5%	3.2%	3.4%

- Among patients who received their first diagnosis of SM in 2021, nearly two-thirds (62.2%) of advanced SM patients had evidence of a bone marrow biopsy between 2015 and 2022 (Figure 3)
- However, only approximately one-third of ISM patients (35.5% of higher symptom-burden ISM, 32.3% of lower symptom-burden ISM) had evidence of bone marrow biopsy during the same time period (Figure 3)

Figure 3. Evidence of Bone Marrow Biopsy 2015 to 2022 In SM Patients with First Diagnosis in 2021



- SM-specific treatment use among patients diagnosed in 2021 was limited and highly variable across treatments and by SM subtype (Figure 4)
- Healthcare services utilization also varied. Notably, 57% of advanced SM patients had a visit to a hematology oncologist (HemOnc), medical oncologist (MedOnc), or hematologist (Hem), whereas only 33% of higher symptom burden ISM and 28% of lower symptom-burden ISM patients visited these providers during 2021 (Figure 5)
- Additionally, 36% of lower symptom-burden ISM, 46% of higher symptom-burden ISM, and 47% of advanced SM patients were admitted to the emergency room (ER) at least once during 2021 (Figure 5)

Figure 4. Observed Therapy Use in 1-Year Period (2021)

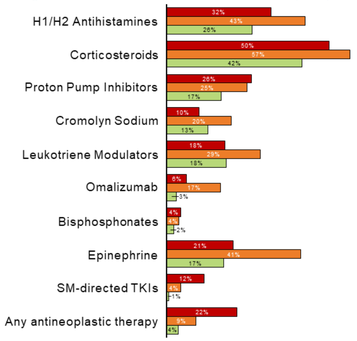
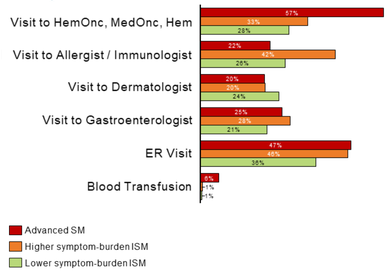


Figure 5. Observed Events in 1-Year Period (2021)



- Figure 6 shows the observed use of SM-directed TKIs in 2021, based on whether the patient had evidence of a bone marrow biopsy: 14.4% of advanced SM patients and 5.5% of higher symptom-burden ISM patients with evidence of a bone marrow biopsy had an SM-directed TKI in 2021, compared to 7.5% of advanced and 3.7% of higher symptom-burden ISM patients without evidence of bone marrow biopsy; Few lower symptom-burden ISM patients received TKIs, regardless of bone marrow biopsy status (0.6% each)
- Similar patterns of use of antineoplastic agents were observed (Figure 7). 24.7% of advanced SM, 10.7% of higher symptom-burden ISM, and 4.6% of lower symptom-burden ISM with evidence of bone marrow biopsy vs. 17.6%, 7.9%, and 3.2%, respectively, without bone marrow biopsy had evidence of antineoplastic agents in 2021

Figure 6. Use of SM-directed TKIs in 2021 by Evidence of Bone Marrow Biopsy

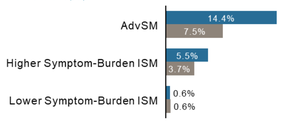
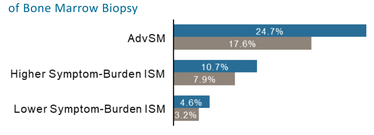
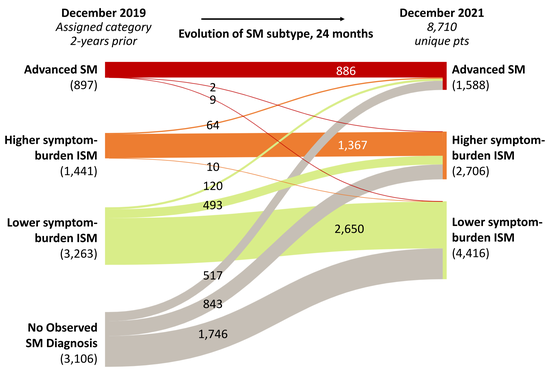


Figure 7. Use of Any Antineoplastic Agent in 2021, by Evidence of Bone Marrow Biopsy



- Figure 8 shows the disease severity at the end of 2021, and the subtype 24 months prior (i.e., December 2019)
- 18.8% of patients with lower symptom-burden ISM in December 2019 migrated to ISM-higher or advanced SM over the 24-month (December 2019 - December 2021) interval
- Across all ISM types, 3.9% of patients progressed to advanced SM over the 24-month interval
- Among those patients who emerged with advanced SM over the 24-month interval ending December 2021 (N=701), 26.2% progressed from ISM-Lower or ISM-higher while 73.8% appeared as de novo diagnoses

Figure 8. SM Subtype Categorization, Worsening, and Progression Over 24 Months



Limitations

- Approximately 35% of qualifying patients did not have a SM diagnosis 2 years prior, possibly due in part to the recency of the SM ICD-10 codes and raising concerns regarding timely diagnosis
- This algorithm has been developed with expert clinical input, however, inherent limitations of claims and a single ICD-10 diagnosis code for SM leave some ambiguity around the true clinical diagnosis of these patients

Conclusions

- This analysis utilized a large US claims dataset and a novel algorithm to identify patients with SM and describe patterns of disease progression and worsening over a 24-month period and 12-month resource utilization
- The analysis reflects the accumulation of severe symptoms over time by a meaningful subset of patients
- There is wide heterogeneity in clinical phenotypes among patients with ISM, leading to treatment differences
- 30% of patients with ISM were categorized as higher symptom-burden ISM, requiring greater use of symptom-directed and disease-specific therapies
- Finally, the proportion of advanced SM patients on FDA-approved SM-directed TKI therapies remains low, highlighting large unmet clinical treatment needs in this rare disease field

References

1. Valent, P. Akin, C, Gleixner, Evet al. Multidisciplinary challenges in mastocytosis and how to address with personalized medicine approaches. *International journal of molecular sciences*, 2019; 20(12), 2976.
2. Shomali W, Gotlib, J. The new tool "KIT" in advanced systemic mastocytosis. *Hematology 2014, the American Society of Hematology Education Program Book*, 2018(1), 127-136.
3. Pardanani, A. Systemic mastocytosis in adults: 2019 update on diagnosis, risk stratification and management. *American journal of hematology*, 2019; 94(3), 363-377.
4. Jaffe ES, Metcalfe DD, Akin C, et al. In: Swerdlow S, Campo E, Harris NL, Jaffe E, Pileri S, Stein H, Thiele J. eds. Mastocytosis, in WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues. Lyon: International Agency for Research and Cancer (IARC); 2017:62-69.
5. Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016;127:2391-2405.
6. Cohen, S. S., Skovbo, S., Vestergaard, H., et al. Epidemiology of systemic mastocytosis in Denmark. *British Journal of haematology*, 2014;166(4), 521-528.

Disclosures

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