Poster #149

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

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SCAN ME

Background/Objectives

- 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 SM subtypes and worsening within.[4,5]
- Comprehensive testing and specialist care management is needed to ensure accurate diagnosis and treatment of patients with SM.
- **The objectives of this study were to identify SM cases and assess disease progression or worsening among patients with ISM and to describe treatment utilization and unmet treatment need in the era of KIT inhibitors, especially among those with ISM.**

Methods

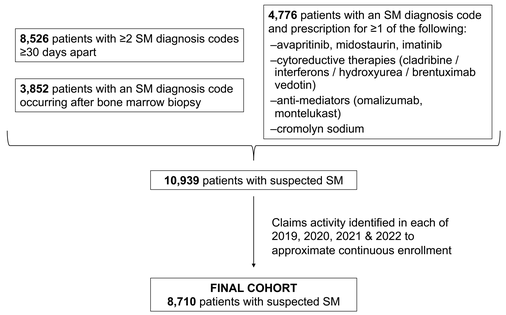
Cohort Identification

- This analysis utilized a large nationally representative United Stated (US) claims database with 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 claims-based algorithm based on WHO diagnostic criteria (2016)[5] was used to identify patients.
- Patients were selected if they fulfilled 1 or more 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; OR
  - 1 SM diagnosis code in any setting of care & ≥ 1 prescription claim for an SM-specific treatment (avapritinib, midostaurin, imatinib, cladribine, interferons, hydroxyurea, brentuximab vedotin, omalizumab, montelukast, or cromolyn sodium).
- Qualifying patients were 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 or worsening

Figure 1. Patient Cohort Identification



Results

- 8,710 patients with SM qualified for analysis (Figure 1), including 1,588 advanced SM, 2,706 ISM-higher, and 4,416 ISM-lower patients (Table 1). This analysis focuses on those patients who had ISM at the start of the study period.
- Mean age at diagnosis among ISM patients was 48 years.
- Racial breakdown strongly biased towards whites (86.5% of ISM) but may reflect inequities regarding access to healthcare rather than true underlying epidemiologic differences.
- Female predominance (71.6% of ISM) aligns with findings from other claims-based studies.[6]
- A majority of patients were enrolled in commercial insurance plans (69.1% of ISM).

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 organ involvement ▪ ≥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

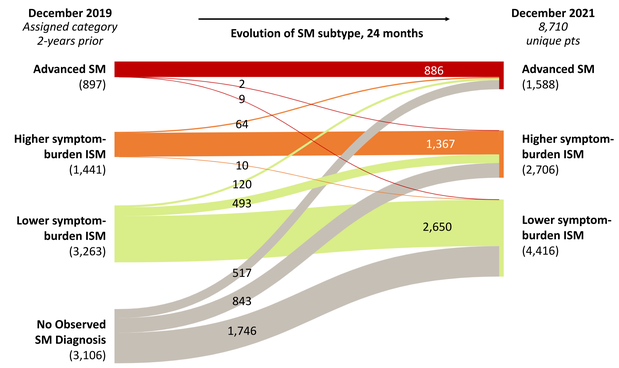
*D47.09 Other mast cell neoplasms of uncertain behavior, C96.20 Malignant mast cell neoplasm, unspecified, C96.22 Mast cell sarcoma, C96.29 Other malignant mast cell neoplasms

Table 1. Baseline Patient Demographics, in 2021

Parameter	All ISM (2021)	Higher Symptom-burden ISM (2021)	Lower Symptom-burden ISM (2021)
Number of Unique Patients	7,122	2,706	4,416
Age at first SM diagnosis			
Mean (standard deviation)	48.0 (18.4)	47.5 (16.9)	48.4 (19.2)
Age at end of 2021 (%)			
<18	5.5%	3.5%	6.7%
18 – 39	22.0%	23.8%	20.9%
40 – 54	27.9%	30.0%	26.6%
55 – 65	23.2%	23.8%	22.8%
>65	21.4%	18.9%	23.0%
% Male	28.4%	25.1%	30.4%
Race / Ethnicity (%)			
Unknown	46.9%	44.3%	48.5%
Among known:			
White	86.5%	87.3%	85.9%
Hispanic or Latino	5.0%	5.0%	4.9%
Black/African American	3.4%	3.6%	3.3%
All Other	5.1%	4.0%	5.9%
Region (%)			
Northeast	20.1%	21.1%	19.5%
South	32.2%	31.3%	32.7%
Midwest	21.7%	22.9%	20.9%
West	21.3%	20.0%	22.1%
Unknown	4.7%	4.8%	4.7%
Payer (%)			
Commercial	69.1%	69.2%	69.0%
Medicare Advantage	20.7%	7.4%	6.6%
Managed Medicaid	6.9%	20.1%	21.0%
Other or Unknown	3.3%	3.2%	3.4%

- Figure 3 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 (15.1%) or advanced SM (3.7%) 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 3. SM Subtype Categorization, Worsening, and Progression Over 24 Months



- SM-related treatment use among patients in the full year 2021 was highly variable across treatments and by SM subtype, and the highest use of corticosteroids and epinephrine was observed in patients who worsened from low-symptom to high-symptom ISM (Figure 4).
- Healthcare services utilization also varied. Notably, ISM patients were significantly less likely than AdvSM patients to have encountered a hematologist oncologist (HemOnc), medical oncologist (MedOnc), or hematologist (Hem) in a 1-year interval, and patients who progressed from ISM to AdvSM were the most likely to have visited these specialties (Figure 5).
- Additionally, visits to gastroenterologists and emergency rooms were also significantly elevated in patients who progressed from ISM to AdvSM, which likely reflects increased GI symptom burden and/or anaphylaxis. Across ISM groups, patients were more likely to visit an Allergist/Immunologist than those with AdvSM (Figure 5).

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

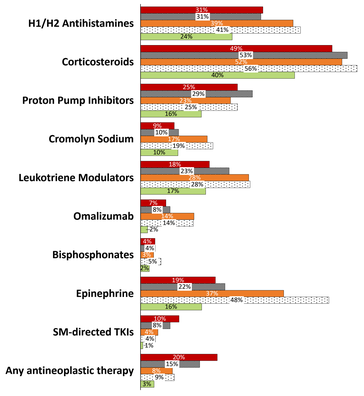
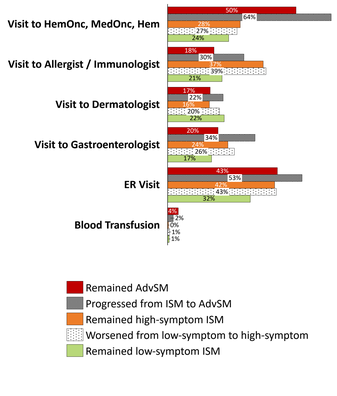


Figure 5. Observed Events in 1-Year Period (2021)



- Figure 6 shows the observed use of SM-directed TKIs in 2021, based on whether the patient had evidence of a bone marrow biopsy (BMB): 12.8% of advanced SM patients and 4.7% of higher symptom-burden ISM patients with evidence of a BMB had an SM-directed TKI in 2021, compared to 6.0% of advanced and 4.3% of higher symptom-burden ISM patients without evidence of BMB. Few lower symptom-burden ISM patients received TKIs, regardless of BMB status (0.6-0.7% each); similar trends were observed when evaluating any antineoplastic agent (Figure 7).
- Notably, SM patients with evidence of BMB across subtypes were more likely to have utilized advanced, SM-directed therapies versus patients without evidence of BMB (Figures 6-7), indicating that proper workup inclusive of BMB may ultimately drive differences in clinical decision-making.

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

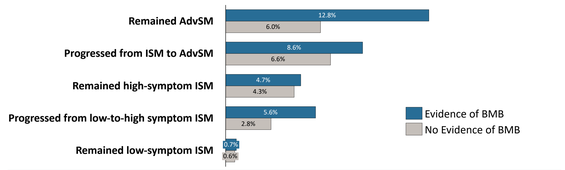
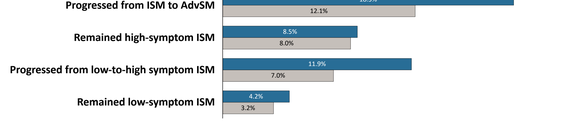


Figure 7. Use of Any Antineoplastic Agent in 2021, by Evidence of Bone Marrow Biopsy



Conclusions

- This analysis utilized a large US claims dataset to identify patients with SM and describe patterns of disease progression and worsening over a 24-month period and 12-month resource utilization. 38% of patients with ISM were categorized as higher symptom-burden ISM, requiring greater use of symptom-directed and disease-specific therapies.
- 18.8% of patients with lower-symptom burden ISM worsened or progressed during the 24-month study period. The analysis reflects the accumulation of severe symptoms over time by a meaningful subset of patients.
- Despite multiple available symptom-directed therapies, an unmet need remains for SM patients that continue to have worsening symptoms and/or disease progression.

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Disclosures

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