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

Sudipto Mukherjee, Douglas J. Cattie, Naveen Panjwani, Daniel Shabaneh, Teresa Green

Background/Objectives

- Systemic mastocytosis (SM) is a rare disease driven by the KIT D816V mutation in ~95% of patients. 
- ~95% of patients with SM have non-advanced stages of disease (indolent SM) and remaining SM, and the standard of care is focused on symptom management. 
- While World Health Organization (WHO) criteria differentiate between subtypes of mastocytoses, there remains a lack of understanding of patterns of disease progression between SM subtypes and worsening outcomes.
- 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 SM and describe treatment utilization and out-of-pocket treatment need in the era of JAK inhibitors, especially among those with ISM.

Methods

- Cohort Identification
- This analysis utilized a large nationally representative United States (US) claims database with patients with commercial, Managed Medial, and Medicare Advantage coverage, 2015-2020. Patients were included if they had claims in each year 2019-2021, and patients were enrolled if they had claims in each year 2018-2021, and patients were continuously enrolled in each year of the study period.
- A claims-based, time-varying cohort identified using ICD-10-CM code (D47.02, C96.21, C94.3X) ≥30 days apart in any setting of care.
- Bone marrow biopsy followed by a SM diagnosis claim code in any setting of care.
- 1 SM diagnosis code in any setting of care & 1 prescription claim for an ISM-specific treatment (aprepitant, lansoprazole, mesna, cladribine, interferon, hydroxyurea, brentuximab vedotin, omacetaxine, meglumine, or intravenous corticosteroids).
- 1 ISM diagnosis & 1 prescription claim for any JAK inhibitor (ruxolitinib, fedratinib, ponatinib).
- 1 ISM diagnosis code (D47.02) occurring following an ambiguous mast cell neoplasm ≥2 SM (D47.02)
- ≥1 SM codes (C94.3x, C96.21, D47.02) in addition to ≥1 associated hematologic diagnosis (WHO criteria code in order to capture ISM patients).

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

Results

- 8.710 patients with ISM qualified for analysis (Figure 1), including 1,588 advanced SM, 2,706 lower SM, and 4,416 ISM lower SM patients (Table 1). This analysis focuses on those patients who had ISM at the start of the study period.
- Mean age at diagnosis among SM patients was 48 years.
- Among strong symptomists identified whites (85.8% of SM) but may reflect inequities regarding access to healthcare rather than true underlying epidemiologic differences.
- Partial remission/Partial response (7.4% of ISM) aligns with findings from other claims-based studies.
- A majority of patients were enrolled in commercial insurance plans (69.1% of ISM).

- Figure 3 shows the disease severity at the end of 2021, and the subtype 24 months prior (i.e., December 2019) (2021) (2021). 18% of patients with lower symptom burden SM in December 2019 progressed to ISM-higher burden SM (5.1%) or advanced SM (7.9%) 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 (Nov–Dec), 28.2% progressed from ISM-higher burden SM while 7.3% appeared as de novo diagnoses.

- Figure 4 shows the observed use of SM-directed TKIs in 2021, based on whether the patient had a history of ISM at the start of the year. 54% of SM patients and 4.7% of higher symptom burden SM 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 SM patients without evidence of BMB. Few (<3%) of patients with ISM-higher burden SM (1.9%) or ISM-low symptom burden SM (2.2%) received SM-directed TKIs. Similar trends were observed when evaluating any antineoplastic agent.

- 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 (Figure 4), indicating that proper workup including of BMB may ultimately drive differences in clinical decision-making.

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 resource utilization. 38% of patients with ISM were categorized as higher symptom burden ISM, ISM-higher burden SM, suggesting greater use of symptom-directed and disease-specific therapies.
- 18.9% of patients with lower symptom burden ISM worsened during the 24-month study period. This 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.

Table 1: Baseline Patient Demographics, in 2021

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All SM</th>
<th>Lower Symptom-Burden ISM</th>
<th>Higher Symptom-Burden ISM</th>
<th>Lower Symptom-Burden SM</th>
<th>Higher Symptom-Burden SM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Unique Patients</td>
<td>8,710</td>
<td>4,416</td>
<td>2,706</td>
<td>8,526</td>
<td>2,706</td>
</tr>
<tr>
<td>Median (25%, 75%) Age at First SM Diagnosis</td>
<td>48 (33, 64)</td>
<td>48 (33, 64)</td>
<td>48 (33, 64)</td>
<td>48 (33, 64)</td>
<td>48 (33, 64)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>4,816 (55.4%)</td>
<td>2,474 (46.4%)</td>
<td>2,342 (46.0%)</td>
<td>5,103 (60.1%)</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td>White</td>
<td>6,648 (76.5%)</td>
<td>3,771 (69.0%)</td>
<td>2,977 (55.7%)</td>
<td>7,276 (86.3%)</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>163 (1.9%)</td>
<td>94 (1.7%)</td>
<td>69 (1.3%)</td>
<td>283 (3.4%)</td>
</tr>
<tr>
<td></td>
<td>Black or African American</td>
<td>883 (10.2%)</td>
<td>511 (9.4%)</td>
<td>372 (6.9%)</td>
<td>1,317 (15.5%)</td>
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<tr>
<td></td>
<td>Hispanic or Latino</td>
<td>246 (2.8%)</td>
<td>187 (3.4%)</td>
<td>59 (1.1%)</td>
<td>600 (7.1%)</td>
</tr>
<tr>
<td></td>
<td>All Other</td>
<td>493 (5.7%)</td>
<td>287 (5.4%)</td>
<td>206 (3.8%)</td>
<td>703 (8.3%)</td>
</tr>
<tr>
<td></td>
<td>Assigned category</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>December 2019</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Progressed from ISM to AdvSM</td>
<td>2%</td>
<td>3%</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>Remained low-symptom ISM</td>
<td>39%</td>
<td>44%</td>
<td>42%</td>
<td>44%</td>
</tr>
<tr>
<td></td>
<td>Remained high-symptom ISM</td>
<td>24%</td>
<td>23%</td>
<td>21%</td>
<td>22%</td>
</tr>
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<td>22%</td>
</tr>
</tbody>
</table>

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

- Remained AdvSM
- Progressed from ISM to AdvSM
- Remained low-symptom ISM
- Remained high-symptom ISM
- Remained ISM

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

- Remained AdvSM
- Progressed from ISM to AdvSM
- Remained low-symptom ISM
- Remained high-symptom ISM
- Remained ISM

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