Poster #4783

Systemic Mastocytosis Patient Experience from Mast Cell Connect, the First Patient-Reported Registry for Mastocytosis

Philina Lee, PhD[1]; Tracy I. George, MD[2]; Hongliang Shi, MS[1]; Erica K. Evans, PhD[1]; Teghpal Singh, PhD[1]; Anthony L. Boral, MD, PhD[1]; Vanessa Rangel Miller, MS, MBA[3];Srdan Verstovsek, MD, PhD[4]

[1]Blueprint Medicines, Cambridge, MA; [2]Department of Pathology, University of New Mexico School of Medicine, Albuquerque, NM; [3]AltaVoice (formerly PatientCrossroads), San Mateo, CA; [4]Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

BACKGROUND

- Systemic mastocytosis (SM) is a rare, underrecognized hematologic disorder characterized by excess mast cells in the bone marrow and other organs.[1,2,3]
- Patients with SM often present with debilitating symptoms that are not effectively addressed by current treatments.[1,4,5] The KIT D816V mutation is a common genetic driver found in most cases.[3, 6–10]
- Little is known about the patients' journey, their perspective on the burden of disease, and real-world treatment approaches for SM.
- Systematically characterizing the natural history of SM and its impact on patients will facilitate the development of new therapies.

THE MAST CELL CONNECT REGISTRY

- Mast Cell Connect (NCT02620254, www.mastcellconnect.org), the first patient-reported registry for mastocytosis, began enrolling on Dec 1, 2015.

Key study objectives

- To facilitate the development of new therapies by improving collective understanding of the natural history of mastocytosis and its impact on patients, as well as increasing participation in clinical trials.
- Here we present early data from Mast Cell Connect.

METHODS

- The Mastocytosis Society, expert physicians, and media coverage enabled rapid participant enrollment.
- Participants registered on a secure online portal and completed a 25-item survey providing demographic, disease, and treatment information. This survey was developed specifically for Mast Cell Connect and incorporated standard questions used in rare disease patient registries, questions from the EORTC QLQ-C30 quality of life questionnaire, and questions tailored to patients with mastocytosis.
- 'Site-agnostic' enrollment enables broader participation and collection of real-world data, particularly in the US, where many patients are seen in the community setting.
- Inclusion criteria were a diagnosis of SM or cutaneous mastocytosis (CM). Participants reporting diagnoses of both SM and CM were categorized as SM participants.
- Diagnoses were self-reported; however, participants were asked to provide medical reports that will be used to confirm diagnoses in the future.
- The study is IRB-approved and informed consent was required to join.

RESULTS

Participant demographics

- At time of data cut-off (September 30, 2016), 208 participants had joined Mast Cell Connect.
- The majority of participants were female (74%) and reported a diagnosis of SM (66%) (Table 1).
- SM participants frequently reported concomitant CM, seen in 37% of indolent SM (ISM), 11% of SM subtype unknown, and 1% of advanced SM (AdvSM).
- Subsequent analyses focused on participants with SM.

Table 1. Participant demographics

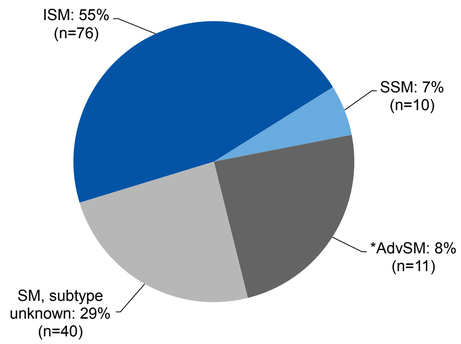
	All[1] (n=208)	SM (n=137)	CM (n=47)[2]
Age, median (range)	46 (0–77)	50 (0–77)	31 (2–68)
Gender, n (%)			
Male	54 (26)	29 (21)	23 (49)
Female	154 (74)	108 (73)	23 (49)
Race, n (%)			
White	189 (91)	130 (95)	38 (81)
Country, n (%)			
US	187 (90)	123 (90)	40 (85)
Canada	8 (4)	5 (4)	2 (4)
Other[3]	13 (6)	9 (7)	4 (9)

[1]Ten participants reported diagnoses other than SM or CM; 14 participants did not report their diagnosis. [2]All CM participants did not answer all demographic questions. Percentages were calculated based on the total number of participants. [3]Other countries include the UK (n=3), Australia and Brazil (n=2); Belgium, Denmark, France, Italy, New Zealand, and Switzerland (n=1).
SM, systemic mastocytosis; CM, cutaneous mastocytosis

SM subtypes are consistent with prior studies

- The frequency of SM subtypes amongst participants was generally consistent with published studies.[1]
- Many SM participants (29%) did not know their subtype, information that is important to assess prognosis and guide treatment decisions (Figure 1).

Figure 1. Frequency of SM subtypes



* AdvSM was comprised of aggressive SM (n=7), SM with an associated hematologic neoplasm (n=3), and mast cell leukemia (n=1).
AdvSM, advanced SM; ISM, indolent SM; SSM, smoldering SM

SM participants reported an 8-year diagnostic odyssey

- The median time from SM symptom onset to diagnosis was 8 years (Figure 2; Table 2).
- Participants saw a median of three specialists prior to diagnosis, including specialists in dermatology (69%), allergy/immunology (67%), hematology/oncology (64%), and general practitioner/internal medicine (63%).
- Diagnoses of SM were made most frequently by specialists in dermatology (39%), allergy/immunology (25%), and hematology/oncology (23% for all SM, 73% for AdvSM).
- Diagnosis frequently involved bone marrow (90%), serum tryptase (88%), and KIT mutation testing (64%).

Figure 2. Age at symptom onset and diagnosis of SM

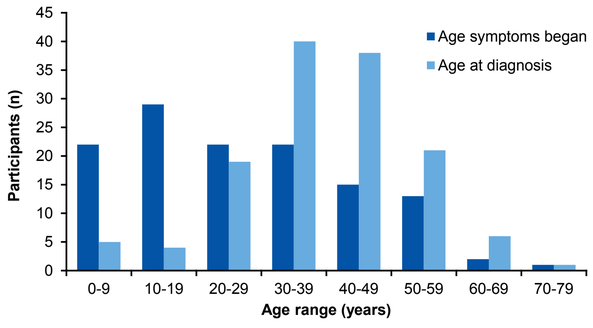


Table 2. Time from symptom onset to diagnosis

	SM (n=125)[1]	ISM (n=68)	SSM (n=10)	AdvSM (n=11)
Median (years)	8	9	9	4
Mean (SD)	12 (12)	12 (11)	13 (13)	13 (15)

[1]Number of SM participants who responded to this question.
AdvSM, advanced SM; ISM, indolent SM; SD, standard deviation; SSM, smoldering SM

SM participants are affected by a range of bothersome symptoms

- Participants reported symptoms that are generally consistent with prior studies.[11–14]
- The most common symptoms (affecting ≥50% of all SM participants) were fatigue (71%), difficulty concentrating (60%), pain (other than abdominal: 54%, abdominal: 53%), and difficulty sleeping (53%) (Table 3).
- Several gastrointestinal symptoms, difficulty concentrating, difficulty sleeping, anxiety, and depression tended to be reported more frequently in AdvSM participants.

Table 3. Frequency of participants experiencing moderately to severely bothersome symptoms within the past year (%)

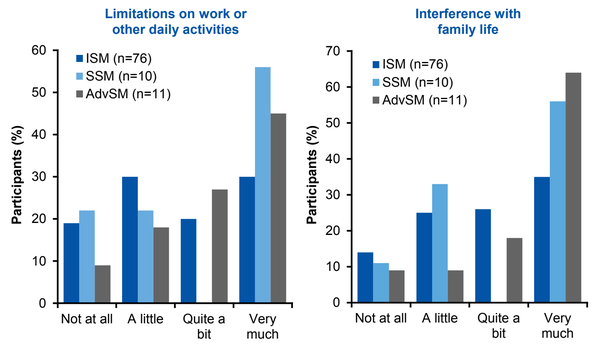
	SM (n=137)	ISM (n=76)	SSM (n=10)	AdvSM (n=11)
Systemic symptoms				
Fatigue/tiredness*	71%	71%	60%	82%
Pain (other than abdominal)	54%	54%	50%	64%
Headache	41%	46%	30%	27%
Sweating	34%	34%	20%	45%
Swelling	32%	34%	10%	36%
Anaphylaxia	30%	32%	40%	27%
Difficulty breathing	26%	29%	30%	27%
Gastrointestinal symptoms				
Abdominal pain*	53%	54%	30%	73%
Bloating	47%	50%	30%	45%
Diarrhea*	45%	42%	50%	45%
Nausea*	41%	42%	40%	82%
Flatulence	32%	30%	20%	36%
Vomiting*	19%	14%	30%	55%
Skin symptoms				
Itching*	44%	43%	40%	55%
Flushing*	40%	41%	40%	36%
Skin changes*	38%	42%	10%	45%
Other impacts				
Difficulty concentrating	60%	59%	50%	91%
Difficulty sleeping	53%	54%	40%	73%
Anxiety	38%	34%	30%	64%
Depression	31%	30%	10%	55%

*Symptoms measured in the advSM-SAF, a patient-reported outcomes instrument in development.
AdvSM, advanced SM; ISM, indolent SM; SSM, smoldering SM

SM impacts daily living

- Across all subtypes of SM, ≥50% of participants reported that SM impacts 'quite a bit' or 'very much' on their work or other daily activities and family life (Figure 3).
- There was a trend for greater impact to be reported more often by AdvSM participants.

Figure 3. SM impacts daily living



AdvSM, advanced SM; ISM, indolent SM; SSM, smoldering SM

Medication use is focused on addressing symptoms

- Most SM participants, across all subtypes, are currently using symptom-treating therapies (Table 4).
- 20–30% of participants with AdvSM and SSM (and a small number of participants with ISM) are currently using therapies to reduce mast-cell burden.
- The use of imatinib (7%) was higher than expected, as it is not indicated for patients with the KIT D816V mutation.[15]

Table 4. Frequency of participants currently using each medication (%)

	SM (n=137)	ISM (n=76)	SSM (n=10)	AdvSM (n=11)
Symptom treating				
Anti-histamines, H1 blockers	85%	83%	90%	82%
Anti-histamines, H2 blockers	70%	70%	60%	82%
Leukotriene inhibitor	39%	38%	50%	45%
Cromolyn sodium	35%	36%	20%	27%
Epinephrine injection	34%	36%	30%	27%
Topical cream for skin rash	9%	12%	20%	0%
Oral steroids	9%	9%	30%	18%
Omalizumab	7%	9%	0%	18%
Mast-cell burden				
Imatinib mesylate	7%	3%	20%	36%
Inteferon-alpha	1%	0%	0%	18%
Midostaurin	1%	0%	0%	18%
Hydroxyurea	1%	1%	10%	0%
Cladribine	1%	0%	10%	0%
Other				
Tacrolimus or cyclosporine	1%	3%	0%	0%

AdvSM, advanced SM; ISM, indolent SM; SSM, smoldering SM

CONCLUSIONS AND NEXT STEPS

- Over the 9-month period from initiation of enrollment to data cut-off, 208 participants joined Mast Cell Connect, suggesting the mastocytosis community is highly motivated to participate in research.
- Participants reported a diagnostic odyssey of 8 years from symptom onset to diagnosis, indicating that SM is largely underrecognized. Efforts to speed the time to diagnosis of SM are urgently needed to improve patient care.
- Despite frequent use of symptom-treating medications, many patients suffer from debilitating symptoms and limitations on daily activities. Novel therapies are needed to improve quality of life and outcomes.
- Continued enrollment and additional surveys are planned to augment these findings and inform the development of new therapies.
- Continued collaboration between researchers, patient advocates, and industry is needed to advance care and the development of new treatments for patients with SM.

For more information

For more information, please visit www.mastcellconnect.org or contact us at patients@blueprintmedicines.com.

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Disclosures
Philina Lee, Hongliang Shi, Erica K. Evans, Teghpal Singh and Anthony L. Boral are employees and stockholders at Blueprint Medicines. Tracy George is a consultant for Blueprint Medicines, Novartis, Incyte, GLG, Wiley Blackwell, Seattle Genetics, and Celgene, receives research funding from Allakos and Celgene, patents and royalties from Wolters Kluwer, American Registry of Pathology, and UptoDate, and is a member of the board of directors or advisory committees for Celgene. Vanessa Rangel Miller is an employee and stockholder at AltaVoice (formerly PatientCrossroads). Srdan Verstovsek has no relevant financial relationships to disclose.

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