Healthcare Burden of Patients Newly Diagnosed with Moderate to Severe Non-Advanced Systemic Mastocytosis Using a Real-world Database of US Health Plan Members

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Background

- Systemic mastocytosis (SM) is a rare mast cell neoplasm primarily driven by KIT D816V mutation.^{1,2} Uncontrolled mast cell proliferation can cause debilitating symptoms including skin lesions, anaphylaxis, organ damage, and diarrhea.³
- As per the updated World Health Organization (WHO) classification in 2016, SM is divided into advanced SM (aggressive SM [ASM], SM with associated hematological neoplasm [SM-AHN], and mast cell leukemia [MCL]) and non-advanced SM (non-AdvSM, including indolent SM [ISM] and smoldering SM [SSM]).^{1,4}
- There are currently no therapies available that are specifically designed to target D816V mutation, the underlying driver of SM.

Methods

STUDY DESIGN AND DATA SOURCE

- A retrospective cohort study with 12-month pre-and post-index periods was conducted using the PharMetrics[®] Plus database from Oct 1, 2015 to Sept 30, 2019 (study period).
- Newly diagnosed patients with SM were identified from Oct 1, 2016 to Sep 30, 2018 (selection window); index date was the date of the first observed SM diagnosis code.
- To derive a non-SM comparison cohort, a 1% random sample of health Baseline patient characteristics, all-cause HCRU, and costs were plan claimants was extracted from the source dataset; a randomly assessed in the 12-month pre-index period. selected pharmacy or medical claim was defined as the index date for these patients.

SAMPLE SELECTION

- An algorithm based on concomitant conditions, procedures, and medications was used to identify non-AdvSM patients using the following steps:
- Step 1: Identification of overall SM sample
- Patients with ≥1 ICD-10-CM code for SM in any position (D47.02 **OR** C94.30 **OR** C94.31 OR C94.32 OR C96.21) during the selection window.

Step 2: Of step 1, exclude adv-SM patients

• Patients who met eligibility criteria for AdvSM (MCL OR SM-AHN OR ASM) any time during the 24-month study period (details described in Poster D3, "Economic Burden of Advanced Systemic Mastocytosis: A Real-World Evaluation of Direct Healthcare Resource Utilization and Costs from a United States Payer Perspective") were excluded.

Step 3: Of step 2, non-advSM patients were identified

- HCRU and costs outcomes over the 12-month pre- and post-index • Upon excluding patients from step 2, this cohort comprised patients who met eligibility period were compared between the two cohorts using McNemar's test criteria for moderate to severe ISM any time during the 24-month study period. for categorical and paired-t test or Wilcoxon-signed rank tests for • Patients were required to meet one of the following criteria: 1. \geq 1 claim of tyrosine kinase inhibitor (TKI) **OR** \geq 1 claim of specific treatment used continuous variables.
- for severe ISM **OR**
- 2. ≥2 medical claims of diagnosis codes used to define symptoms of severe ISM **OR** 3. \geq 1 claim from a list of pharmacy or procedure codes indicating 'moderate antihistamines' OR 'other moderate qualifiers'

Conclusions

LIMITATIONS • Patients with moderate/severe non-AdvSM had significantly higher • No causal relationships can be derived from the findings of this HCRU and associated medical costs in the year before and after diagnosis compared to matched cohort of patients without SM. retrospective observational study. Total medical costs in non-AdvSM patients were driven primarily by

higher pharmacy and medical outpatient costs. • Further research is needed to understand key drivers of medical costs and identify opportunities to decrease the economic burden of disease.

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• The management of patients with moderate to severe non-AdvSM is typically based on symptom control. Treatment is generally limited to anaphylaxis prevention/symptom control/osteoporosis management.¹ Data on burden of non-AdvSM is limited. As non-AdvSM is marked by long-term morbidity and reduced quality of life,^{5,6} assessment of disease burden can help in understanding the unmet need among these patients.

OBJECTIVE: To estimate and compare healthcare resource utilization (HCRU) and medical costs between patients with moderate/severe non-AdvSM and a matched cohort of patients without SM using a large United States (US) claims database.

- The following additional eligibility criteria were applied:
- Subject age ≥18 years at index date
- Continuous health plan enrollment for 12-months preceding and following (including) the index date
- No data quality issues (invalid year of birth, gender or health plan enrollment dates)
- Without ≥1 diagnosis code for SM in the 12-month pre-index period

MEASURES

- All-cause HCRU and direct medical costs were examined over the 12month post-index period (including index date).
 - HCRU categories (proportion and mean number) included pharmacy reported by prescription fills, outpatient including physician office visits, emergency room [ER] visits, lab/pathology tests, radiology exams, surgical services, and ancillary services use and inpatient visits.
- All-cause total direct medical costs included outpatient pharmacy, outpatient medical (physician office visit, ER visit, lab/pathology, radiology, surgical and outpatient ancillary services), and inpatient costs.

STATISTICAL ANALYSIS

- To adjust for potential selection bias, non-AdvSM patients were direct matched (1:1) to a non-SM comparator cohort on age, gender, index year, and Charlson comorbidity index (CCI) score.
- All costs were converted to 2019 USD using the medical component of the Consumer Price Index.

• Categorization of non-AdvSM relied strictly on a claims-based algorithm; while rigorous in its concept and application, the algorithm is subject to the assumptions of objective and consistent coding practices. Implications from the results are limited to the current patient population and may not be generalizable to other commercially or non-commercially insured populations.

ASM: Aggressive SM; CCI = Charlson Comorbidity Index; ER = emergency room; HCRU: healthcare resource utilization; SSM: Systemic mastocytosis; SM-AHN: SM with associated hematological neoplasm; TKI: Tyrosine kinase inhibitor

Results

STUDY SAMPLE

A total of 170 patients with non-AdvSM met the inclusion criteria, with 61% female, mean (\pm SD) age 46 \pm 11, 64/35% commercial insurance/self-insured (Table 1).

Prevalent baseline comorbidities included cancer (28%), anxiety (26%), asthma (16%), and depression (15%) (**Table 1**). Anaphylaxis was observed in 9% non-AdvSM patients.

After direct matching, patients in the two cohorts were well-balanced on age, gender, index year, payer type, and CCI.

TABLE 1. BASELINE CHARACTERISTICS

		Pre-Match		Post-Match		
Characteristics	Non-			Non-		
	AdvSM	Non-SM	P-	AdvSM	Non-SM	P-
	(N=170)	(N=110,362)	value	(N=170)	(N=170)	value
Age, Mean (SD)	46.2 (11.5)	43.4 (13.6)	0.0094	46.2 (11.5)	46.4 (11.5)	0.4831
Female (%)	61.2%	52.2%	0.0196	61.2%	61.2%	NA
Region (%)			0.0038			0.0128
Northeast	24.7%	18.4%		24.7%	19.4%	
Midwest	28.8%	27.8%		28.8%	24.7%	
South	29.4%	41.8%		29.4%	48.8%	
West	17.1%	12.1%		17.1%	7.1%	
Payer Type (%)			0.3180			0.0991
Commercial	64.2%	57.7%		64.2%	54.7%	
Self-insured	34.7%	40.3%		34.7%	42.9%	
Others	1.2%	2.1%		1.2%	2.4%	
Index Year (%)			<.0001			NA
2016	0.0%	13.9%		0.0%	0.0%	
2017	32.9%	48.3%		32.9%	39.2%	
2018	67.1%	37.8%		67.1%	67.1%	
CCI, Mean (SD)	1.2 (1.4)	0.4 (1.0)	<.0001	1.2 (1.4)	1.2 (1.5)	0.7542
Physician specialty (%)^			<.0001			<.0001
Primary care physician	29.4%	16.9%		29.4%	15.3%	
Oncologist/Hematologist	8.2%	0.8%		8.2%	1.2%	
Allergist/Immunologist	10.6%	0.3%		10.6%	0.0%	
Other	51.8%	82.0%		51.8%	83.5%	
Comorbidities (%) *		0.00/	0004		45.00/	
Cancer	28.2%	3.8%	<.0001	28.2%	15.9%	0.0004
Anxiety	25.9%	11.1%	<.0001	25.9%	16.5%	0.0325
Hypertension	21.8%	20.9%	0.7909	21.8%	32.4%	0.0244
Asthma	16.5%	4.7%	<.0001	16.5%	14.1	0.4927
Depression	14.7%	8.0%	0.0013	14.7%	9.4%	0.1282
lests of interest (%)	C EV	0.40/	- 0001	C F0/	0.00/	0 0020
Commentation biopsy	0.570	0.1%	< 0001	0.0%	0.0%	0.0039
Serum Tryptase	44.1%	0.7%	<.0001	44.1%	1.2%	<.0001
Carticoptoroido	E0.6%	20.0%	< 0001		20.20/	0.0167
Antibiotominee	20.0% 27.6%	29.9%	< 0001	20.0% 27.6%	JO.270 10.60/	2.0001
Epinophrine injectore	27.0%	1.0%	< 0001	27.0%	10.0%	< 0001
Aptiloukotrionos	21.170	0.070	~ 0001	27.170 25.20/	U.070 / 70/	< 0001
Montolukast	20.070	J.170 2,10/	< 0001	20.0 /0	4.170 /170/	
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*Top 5 prevalent comorbidities and medications of interest have been presented; ^Physician specialty is measured at index; NA: P-values are not applicable because patients were direct matched on age group, gender, year of index, and CCI (categorical)

Median pre-index medical costs were significantly higher for non-AdvSM patients compared to matched non-SM comparator cohort (Figure 1)

 Total pre-index medical costs were driven by outpatient and pharmacy costs.

FIGURE 1. MEAN (MEDIAN) PRE-INDEX MEDICAL COSTS **BETWEEN NON-ADVSM AND MATCHED NON-SM COHORTS**



P-values are presented only for medians

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Medical costs	Non-AdvSM (N=170)		Non-SM (N=170)		P-value	P-value
	Mean	Median	Mean	Median	(mean)	(methan)
Total	\$24,588	\$9,019	\$14,419	\$4,035	0.0254	<.0001
Pharmacy	\$11,288	\$1,301	\$4,742	\$423	0.0377	0.0006
ER	\$637	\$0	\$725	\$0	0.7696	0.0281
Physician office	\$2,229	\$1,663	\$1,267	\$672	<.0001	<.0001
Lab/Pathology	\$1,266	\$491	\$532	\$182	0.0003	<.0001
Radiology	\$1,055	\$358	\$1,157	\$113	0.8003	0.0427
Surgical	\$2,433	\$143	\$1,168	\$0	0.0613	0.0801
Ancillary services	\$3,143	\$823	\$3.099	\$89	0.9733	0.0001
Inpatient	\$2,536	\$0	\$1,729	\$0	0.5614	0.6742



OUTCOMES: POST-INDEX HCRU AND COSTS

Proportion of patients with utilization of select medications of interest were significantly higher in the non-AdvSM cohort compared to non-SM controls during 1-year follow-up (**Figure 2**).

 Common medications among non-AdvSM vs. controls included H1 antihistamines (20% vs. 9%) and leukotriene antagonists (26% vs. 6%) (both

P<0.01); 29% (vs. 1%) filled a prescription for epinephrine (P<0.001).

FIGURE 2. PROPORTION OF PATIENTS WITH ≥1 PRESCRIPTION OF **MEDICATIONS OF INTEREST BETWEEN NON-ADVSM AND** MATCHED NON-SM COHORTS



number of prescription fills and outpatient service utilization among non-AdvSM vs. non-SM patients (Figure 3). **3. MEAN POST-INDEX ALL-CAUSE HCRU BETWEEN**

AND MATCHED NON-SM COHORTS



Median medical costs during the 1-year post-index period were higher for non-AdvSM vs. non-SM patients (**Table 2**).

Mean \pm SD (median) post-index total medical costs were \$24,588 \pm 51,385 (\$9,019) vs. \$14,419±33,449 (\$4,035) (*P*<0.001).

Pharmacy (45.9%) and outpatient medical costs (43.8%) accounted for a majority of follow-up costs among non-AdvSM patients.

TABLE 2. MEAN +/- SD AND MEDIAN ALL-CAUSE MEDICAL COSTS **BETWEEN NON-ADVSM AND MATCHED NON-SM COHORTS**

References: ¹ Pardanani A. American journal of hematology. 2019 Mar, 94(3):363-77; ² Grootens J et al. EBioMedicine. 2019 May 1, 43:150-8; ³ Schwartz, LB. Immunol Allergy Clin N Am. 2006,26(3):451-463; ⁴Arber DA, et al. Blood. 2016, 127:2391-2405; ⁵Jennings SV, et al. Immunology and Allergy Clinics. 2018 Aug 1,38(3):505-25; ⁶Mesa RA, et al. Results from the TouchStone Survey, In Blood 2020, Nov 5 (Vol 136), presented at Amer Soc Hematology.

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