Utility of a Validated Disease-Specific Measure to Assess Symptomology in Patients with Indolent Systemic Mastocytosis (ISM)

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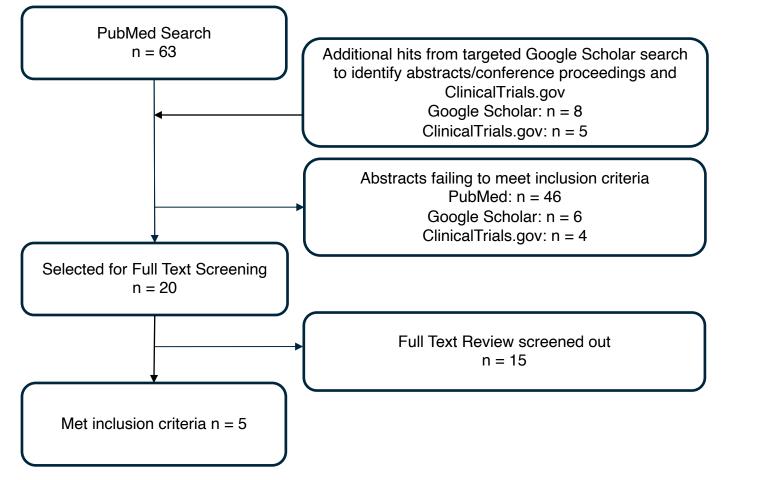
Background

- Systemic mastocytosis (SM) is a rare condition characterized by accumulation of neoplastic mast cells of more than one organ driven by the KIT D816V mutation.¹
- SM manifests as indolent systemic mastocytosis (ISM), smoldering SM (SSM), and advanced SM $(AdvSM).^{2}$
- Non-advanced SM, including ISM and SSM, comprise 90-95% of total cases.³
- ISM is associated with long diagnostic delays, decreases quality of life, and causes debilitating and unpredictable symptoms for patients, including life

Methods

- A targeted review of peer-reviewed literature between 2015 and 2021 was conducted to systematically assess and summarize the development and validation of the ISM-SAF and explore its potential utility (Figure 1).
- The primary objective was to identify and synthesize data from publications reporting patient-level results using the ISM-SAF.
- The search was primarily conducted in PubMed, and supplemented through Google Scholar and Clinicaltrials.gov.
 - Search terms in PubMed included: "systemic mastocytosis," "symptom assessment," "patient reported outcomes," and "quality of life".
 - A targeted Google Scholar search aimed to capture abstracts, posters, and conference proceedings that were not captured in PubMed

FIGURE 1. SEARCH FLOW DIAGRAM FOR **REVIEW OF ISM-SAF**



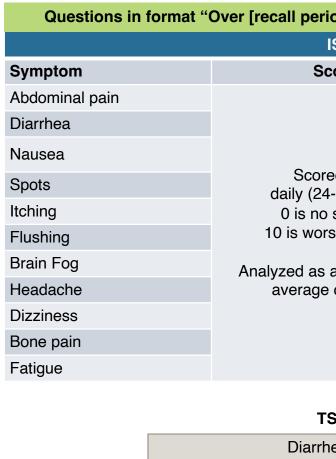
threatening anaphylaxis.⁴

- The ISM symptom assessment form (ISM-SAF) was developed to measure disease symptomology.⁵
- This research assesses and describes the development and validation of the ISM-SAF, a symptom assessment tool developed specifically for ISM patient populations and explore its potential utility.

articles were excluded.

- Clinicaltrials.gov was gueried for ISM trials that are "active, not recruiting," "enrolling by invitation," "recruiting," or "not yet recruiting" and hand screened for those utilizing ISM-SAF.
- Records that utilized the ISM-SAF and reported patient-level outcomes met inclusion criteria. Records that used different symptom assessment tools or did not report patient-level outcomes were excluded from the final review.
- Prioritized outcomes were abstracted from the final sources including study characteristics and psychometric properties.

FIGURE 2. ISM-SAF SYMPTOMS ASSESSED. DOMAINS, AND SCORING



How many times

Conclusions

- The development and validation of the ISM-SAF as a 'fit for purpose' tool to assess disease-related symptom severity in ISM patients in both clinical trial and observational research settings has been documented by peer-reviewed publications.
- Use of a reliable and valid symptom assessment tool that evaluates concepts relevant and important to individuals with a condition is important for determining clinical benefit of new treatments.
- The findings from this review highlight the utility of the ISM-SAF as a valuable tool to assess symptom burden and change in ISM symptoms over time.
- As part of the validation, TSS scores have been shown to correlate well with commonly used measures of health status, quality of life (i.e., SF-12, PGIS).
- Research has shown that a 30% individual percentage decrease in TSS is clinically meaningful improvement in ISM symptoms at the individual level
- The ISM-SAF may offer clinicians a valuable tool to assess symptom severity and potential treatment benefits in clinical practice.

Results from "ISM-SAF" were hand screened for inclusion criteria. Abstracts and clinical trials that include data that were later published in full-text

iod], how severe wa	s your worst [symptom]?"
ISM-SAF	
coring	Groups
	GI domain (GSS) (0 – 30)
ed 0 – 10 I-hour recall) symptoms rst imaginable	Skin domain (SSS) (0 – 30)
a 14-day moving or one-time	Neurocognitive symptoms (0 – 30)
SS (0-110)	
nea Frequency: s did you have diarrh	ea?

Results

ISM-SAF Literature Review Results

- One full-text article on the development of the ISM-SAF, three presentations/publications on the application and validation of the ISM-SAF, and one ongoing clinical trial met the inclusion criteria (**Table 1**).
- The ISM-SAF was developed using best practices for PRO development including clinician and patient input on symptoms, cognitive debriefing interviews with patients, and regulatory feedback.⁵
- The ISM-SAF assesses 11 relevant symptoms: abdominal pain, nausea, diarrhea, spots, itching, flushing, bone pain, fatigue, dizziness, brain fog, and headache (Figure 2) and has been validated in multiple languages.⁴
- In addition to a total symptom score (TSS), reflective of overall disease burden, the ISM-SAF tool allows for an evaluation of GI and skin-specific SM domain scores.

ISM-SAF Utility Results

- The ISM-SAF has been used in multiple research settings randomized controlled trial,^{4,8} prospective observational study,⁶ and a cross-sectional patient survey.⁷
- Psychometric analyses have demonstrated the reliability, validity, and responsiveness of the ISM-SAF (Tables 1 & 2, Figures 3 and 4), and confirmed it is a 'fit for purpose' tool to assess symptom severity in SM patients (**Table 2**)
- The ISM-SAF has been used to:
- Assess the overall severity of SM-specific symptoms, calculated as a TSS at a single point in time (**Table 3**),
- Measure change (i.e., improvement, increased severity) over time in SMspecific symptoms with a 30% reduction in TSS considered clinically meaningful, and
- Differentiate between patients with moderate-severe versus mild SM disease (e.g., moderate-severe SM patients have TSS \geq 28).
- •The ISM-SAF is being used in the ongoing HARBOR clinical trial to assess the effects of a new ISM treatment on SM symptoms.⁸

TABLE 1. STUDY CHARACTERISTICS

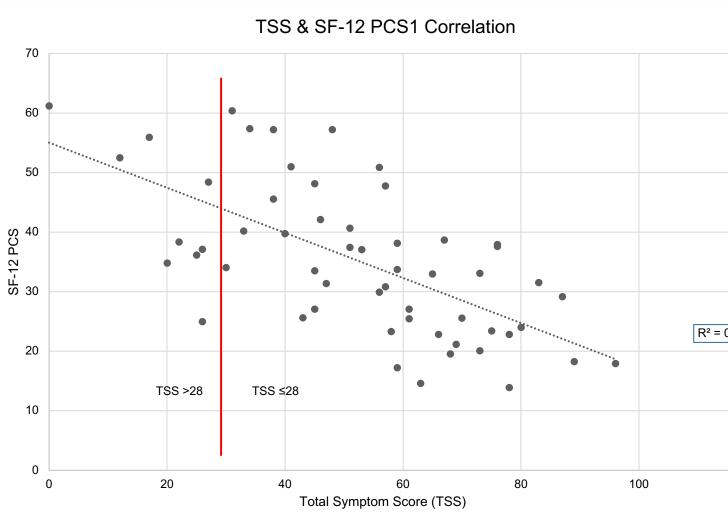
	Study (Author Year)							
Study Characteristics	PIONEER Part 1 (Padilla 2021)	Prospective Observational (Shields 2019)	TouchStone (Mesa 2020)	HARBOR (ongoing P2/3 study)				
NCT Number	NCT03731260	n/a	n/a	NCT04910685				
Study Design	RCT	Prospective Observational	Cross-Sectional	s-Sectional RCT				
Patients	38	103	30 403 (estimated					
Study Duration	Up to 5 years	15 days	1 day Up to 5 years					
Intervention	Randomized to avapritinib or placebo + BSC	n/a	n/a Randomized to BL 263 or placebo +B					
SM Subtype	ISM	ISM or SSM	SM ISM					
Use of Instrument	14-day rolling average	14-day	1-time	Not reported in Clinicaltrials.gov				
Administration Methods	Daily administration in eDiary	Web-based HIPAA- compliant platform (Survey Monkey)	Online survey	Not reported in Clinicaltrials.gov				
Scoring Details	24-hour recall	24-hour recall	Not reported	Not reported in Clinicaltrials.gov				
Utility of ISM-SAF	Symptom Improvement	Symptom Burden	Symptom Burden	Symptom Improvement				
Key Outcomes Reported	Mean Baseline TSS Scores, Reliability (Internal Consistency and Test-Retest) Validity (Construct- Related Validity, Known-Groups Analysis), Sensitivity to change	Reliability (internal consistency, test-retest validity), Validity (Construct-Related Validity, Known-Groups Analysis)	Mean TSS scores, Mean SF-12 MCS, Mean SF-12 PCS	n/a				
Conclusion/ Findings	The ISM-SAF produced reliable, construct valid, and sensitive scores among ISM patients in a randomized clinical trial setting.	These psychometric results support the conclusion that the ISM- SAF can produce trustworthy scores when administered to patients in the target population in that the domain and item scores are reliable, construct-valid, and able to distinguish among clinically unique groups.	This study is the first time the ISM-SAF has been used in a real- world setting and with one-time administration. The TSS scores were correlated with the symptoms assessed; however, further validation work is necessary.	n/a				

Abbreviations: RCT: randomized control trial; BSC: best supportive care;; SSM: smoldering systemic mastocytosis; HIPAA: Health Insurance Portability and Accountability Act; TSS: total symptom score, as calculated from ISM-SAF;SF-12 MCS: 12-item Short Form Survey, mental component score; SF-12 PCS: 12-item Short Form Survey, physical component score - ISM-SAF utility validation continuing in PIONEER Part 2 trial with 204 patients.

TABLE 2. COMPARISON OF RELIABILITY, VALID FROM PIONEER PART 1 AND PROSPECTIVE OB

Study				Part 1 ⁺ (Padi	lla 2021)			Observa	ational S	Study (Sh	ields 2019)		
	seline Scores												
TSS		54.2 10.9						Not reported					
	GSS 10.9 SSS 16.2												
	y: Internal Cor	sistenc		h's Alnha)									
	-		Baseline (n=	• •				CS-AP (n=103)				
•	PopulationBaseline (n=38)TSS0.86					CS-AP (n=103) 0.88							
GSS 0.86								0.78					
5	SSS		0.82			0.67							
Reliability	y: Test-Retest	Reliabil	ity, ICC (95°	% CI)									
Popula	ation		between ba	16 for TSS	and GSS,	PGIS Stable Participants (n=61)							
			n=17 for SS	S)									
TSS 0.956 GSS 0.858						0.962 (0.936-0.977) 0.936 (0.894-0.962)							
	SSS 0.981						0.936 (0.894-0.962) 0.962 (0.937-0.977)						
alidity:	Spearman cor	relation	s of ISM-SA	F total and c	domain s	cores witl	h other mea	· ·		,	ed)*		
Popula	-				e C4D1 ((-		
•	rrent Measure		тее				TSS			CS-AP (n=103)			
										SSS			
	SF-12 PCS SF-12 MCS		-0.226 -0.536	-0.275 -0.368		-0.179 -0.218		-0.631		-0.493 -0.465		-0.308 -0.346	
Ν	MC-QoL		0.695	0.538		0.550		0.849		0.679		0.587	
	PGIS		0.656	0.401		0.618		0.618		0.454		0.446	
alidity: I	Known-Groups	s analys	sis of ISM-S	AF total and	domain	scores ba	ased on PGI	S, MC-Qo	oL, and S	SF-12 sc	ores		
Popula	ation			At time	e C4D1 (n=34)				CS	-AP (n=103)		
	Group		n	TSS mean			SSS mean	n	TSS n	mean	GSS mear	n SS	S mean (S
				(SD)			SD)		(SD)		(SD)		
PGIS	Absent/Minim	al	12	27.1 (10.2)	4.3 (3	-	8.1 (4.0)	41	18.5 (•	3.9 (5.1)		7(3.9)
	Moderate		11	50.4 (12.1)	9.5 (2		2.6 (6.0)	43		(13.0)	5.8 (3.7)		3 (5.3)
	Severe/Very S	Severe	11	55.2 (15.1)	9.7 (6		8.3 (6.5)	18		(20.7)	9.3 (7.7)		8 (5.7)
/IC-QoL	Mild		10	29.5 (10.6)	4.7 (3		0.7 (7.1)	37	16.6 (,	3.4 (3.0)		(4.7)
	Moderate		12	43.4 (16.4)	7.3 (3		2.5 (6.3)	32	29.5 (,	5.1 (3.3)		(5.4)
	Severe		12	55.8 (14.8)	10.7 ((5.8) 1	5.9 (6.5)	33	42.0 (12.0)	8.3 (3.6)	11.0	0 (3.3)
				53.4 (10.8) 10			. ,						
	Mild		11	53.4 (10.8)	10.6 ((3.2) 1	3.8 (7.1)	34	17.2 (11.5)	3.1 (2.6)	5.6	(4.4)
SF-12	Mild Moderate		11 12	53.4 (10.8) 47.8 (19.6)	10.6 (7.6 (6	. ,	3.8 (7.1) 4.2 (5.7)	34 33	17.2 (24.8 (•	3.1 (2.6) 4.7 (3.5)		(4.4) (5.3)
	Moderate Severe		12 11	47.8 (19.6) 29.4 (11.4)	7.6 (6	5.5) 1 3.3) 1	4.2 (5.7) 0.4 (7.7)			8.7)		8.1	· · /
	Moderate	Mean ch	12 11	47.8 (19.6) 29.4 (11.4)	7.6 (6	5.5) 1 3.3) 1	4.2 (5.7) 0.4 (7.7)	33	24.8 (8.7)	4.7 (3.5)	8.1	(5.3)
Sensitivit TSS	Moderate Severe ty to Change: 1 -12.70 (14.93)		12 11	47.8 (19.6) 29.4 (11.4)	7.6 (6	5.5) 1 3.3) 1	4.2 (5.7) 0.4 (7.7)	33 34	24.8 (43.9 (8.7) 13.4)	4.7 (3.5)	8.1	(5.3)
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Sensitivit TSS GSS SSS bbreviations CS rvey, total score ABLE	Moderate Severe ty to Change: I -12.70 (14.93) -3.83 (5.98) -4.07 (5.64)	is population; I indicate strong TS FR (Onlin quest	12 11 nange (SD) CC: interclass correlat (≥0.6) relationships b OM TOU e cross-s tionnaire,	47.8 (19.6) 29.4 (11.4) in biweekly tion coefficient; CI: confi etween ISM-SAF scores CHSTONI Sectional s which in	7.6 (6 5.0 (3 scores fi idence interval ; s and measures E SM F survey cluded	5.5) 1 3.3) 1 rom basel C1D15: cycle 1, da of other instrument PATIEN Of patie the full	4.2 (5.7) 0.4 (7.7) ine to C4D1 ay 15; SD: standard dev ts, conversely, scores s T SURVE ents self-r ISM-SAF	33 34 Not feas	24.8 (43.9 (ible; one ient global imp ate weak (<0.3 SA 202 SA 202	8.7) 13.4) e round of ression of severit 3)relationships be 20) diagno	4.7 (3.5) 8.8 (4.2) 14-day use y; C4D1: cycle 4, day tween ISM-SAF scores	8.1 11. of tool	(5.3) 7 (3.9) tocytosis Quality of I of other instruments
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ensitivit TSS GSS SSS breviations CS vey, total score ABLE Me Key O Re IGURI 2 PCS	Moderate Severe ty to Change: I -12.70 (14.93) -3.83 (5.98) -4.07 (5.64) AP: cross-sectional analys e; * Scores shown in green 3. RESULT A. RESULT Chods Chanse Chods Chanse Chods Chanse Chods Chanse Chods Chanse Chanse Chanse Chods Chanse Chan	is population; I indicate strong S FR Onlin quest burde	12 11 ange (SD) CC: interclass correlationships be OM TOU e cross-settionnaire, ben of SM Mean T 50 ON BET 50	47.8 (19.6) 29.4 (11.4) in biweekly tion coefficient; CI: confi etween ISM-SAF scores CHSTONI Sectional s which in patients in SS NEEN TS SM PATIE	7.6 (6 5.0 (3 scores fi idence interval ; and measures E SM F survey cluded n real-v S AND	5.5) 1 5.3) 1 rom basel C1D15: cycle 1, da of other instrument PATIEN Of patie the full world se Mean (S SF-	4.2 (5.7) 0.4 (7.7) ine to C4D1 av 15; SD: standard dev ts, conversely, scores and and dev T SURVE SURVE SURVE SD) SF-12 44 (1.8) FIGURE SF-12 MO	33 34 Not feas itation; PGIS: Pat shown in red indic Y (MES eportin evalua MCS 3. COR	24.8 (43.9 (ible; one iant global imp ated di SA 202 SA 202 SA 202	8.7) 13.4) e round of ression of severif 3)relationships be 20) diagno isease M ATION I OUCH	4.7 (3.5) 8.8 (4.2) 14-day use (4.7 (3.5) 8.8 (4.2) 14-day use (4.7 (3.5) (4.7) (4.7) (5.7) (4.7) (4.7) (5.7) (4.7) (5.7	8.1 11. of tool	(5.3) 7 (3.9) tocytosis Quality of of other instruments n system PCS AND
Sensitivit TSS GSS SSS Obreviations CS ABLE Me Key O Re IGURI 2 PCS	Moderate Severe ty to Change: I -12.70 (14.93) -3.83 (5.98) -4.07 (5.64) AP: cross-sectional analys e; * Scores shown in green 3. RESULT A. RESULT Chods Chanse Chods Chanse Chods Chanse Chods Chanse Chods Chanse Chanse Chanse Chods Chanse Chan	is population; I indicate strong S FR Onlin quest burde	12 11 ange (SD) CC: interclass correlationships be OM TOU e cross-settionnaire, ben of SM Mean T 50 ON BET 50	47.8 (19.6) 29.4 (11.4) in biweekly tion coefficient; CI: confi etween ISM-SAF scores CHSTONI Sectional s which in patients in SS NEEN TS SM PATIE	7.6 (6 5.0 (3 scores fi idence interval ; and measures E SM F survey cluded n real-v S AND	5.5) 1 5.3) 1 rom basel C1D15: cycle 1, da of other instrument PATIEN Of patie the full world se Mean (S SF-	4.2 (5.7) 0.4 (7.7) ine to C4D1 av 15; SD: standard dev ts, conversely, scores as T SURVE SURVE SURVE SD) SF-12 44 (1.8) FIGURE SF-12 MO	33 34 Not feas itation; PGIS: Pat shown in red indic Y (MES eportin evalua MCS 3. COR	24.8 (43.9 (ible; one iant global imp ated di SA 202 SA 202 SA 202	8.7) 13.4) e round of ression of severif 3)relationships be 20) diagno isease M ATION I OUCH	4.7 (3.5) 8.8 (4.2) 14-day use (4.7 (3.5) 8.8 (4.2) 14-day use (4.7 (3.5) (4.7) (4.7) (5.7) (4.7) (4.7) (5.7) (4.7) (5.7	8.1 11. of tool	(5.3) 7 (3.9) 7 (3.9) occytosis Quality of of other instruments PCS AND TIENTS
Sensitivit TSS GSS SSS Obreviations CS revey, total score ABLE Me Key O Re IGURI 2 PCS	Moderate Severe ty to Change: I -12.70 (14.93) -3.83 (5.98) -4.07 (5.64) AP: cross-sectional analys e; * Scores shown in green 3. RESULT A. RESULT Chods Chanse Chods Chanse Chods Chanse Chods Chanse Chods Chanse Chanse Chanse Chods Chanse Chan	is population; I indicate strong S FR Onlin quest burde	12 11 ange (SD) CC: interclass correlationships be OM TOU e cross-settionnaire, ben of SM Mean T 50 ON BET 50	47.8 (19.6) 29.4 (11.4) in biweekly tion coefficient; CI: confi etween ISM-SAF scores CHSTONI Sectional s which in patients in SS NEEN TS SM PATIE	7.6 (6 5.0 (3 scores fi idence interval ; and measures E SM F Survey cluded n real-v S AND S AND S AND S AND S S AND	5.5) 1 5.3) 1 rom basel C1D15: cycle 1, da of other instrument PATIEN Of patie the full world se Mean (S SF-	4.2 (5.7) 0.4 (7.7) ine to C4D1 av 15; SD: standard dev ts, conversely, scores as T SURVE SURVE SURVE SD) SF-12 44 (1.8) FIGURE SF-12 MO	33 34 Not feas itation; PGIS: Pat shown in red indic Y (MES eportin evalua MCS 3. COR	24.8 (43.9 (ible; one iant global imp ated di SA 202 SA 202 SA 202	8.7) 13.4) e round of ression of severif 3)relationships be 20) diagno isease M ATION I OUCH	4.7 (3.5) 8.8 (4.2) 14-day use (4.7 (3.5) 8.8 (4.2) 14-day use (4.7 (3.5) (4.7) (4.7) (5.7) (4.7) (4.7) (5.7) (4.7) (5.7	8.1 11. of tool	(5.3) 7 (3.9) cocytosis Quality of of other instruments n system PCS AND
Previations CS ABLE Me Key O Re IGURI 2 PCS 130	Moderate Severe ty to Change: I -12.70 (14.93) -3.83 (5.98) -4.07 (5.64) Cores shown in green 3. RESULT Comes ported E 3. CORRI SAMONG T	is population; I indicate strong S FR Onlin quest burde	12 11 ange (SD) CC: interclass correlationships be OM TOU e cross-settionnaire, ben of SM Mean T 50 ON BET 50	47.8 (19.6) 29.4 (11.4) in biweekly tion coefficient; CI: confi etween ISM-SAF scores CHSTONI Sectional s which in patients in SS NEEN TS SM PATIE	7.6 (6 5.0 (3 scores fi idence interval ; and measures E SM F Survey cluded n real-v S AND S AND S AND S AND S S AND	5.5) 1 5.3) 1 rom basel rom basel C1D15: cycle 1, da of other instrument PATIEN Of patie the full world se Mean (S SF-	4.2 (5.7) 0.4 (7.7) ine to C4D1 ay 15; SD: standard dev ay 15; SD: standard dev s, conversely, scores of T SURVE onts self-r ISM-SAF of 5D) SF-12 44 (1.8) FIGURE SF-12 MO 60 40 50 40 50 40 50 40 50 40	33 34 Not feas itation; PGIS: Pat shown in red indic Y (MES eportin evalua MCS 3. COR	24.8 (43.9 (ible; one iant global imp ated di SA 202 SA 202 SA 202	8.7) 13.4) e round of ression of severif 3)relationships be 20) diagno isease M TION I OUCH	4.7 (3.5) 8.8 (4.2) 14-day use (4.7 (3.5) 8.8 (4.2) 14-day use (4.7 (3.5) (4.7) (4.7) (5.7) (4.7) (4.7) (5.7) (4.7) (5.7	8.1 11. of tool	(5.3) 7 (3.9) 7 (3.9) ocytosis Quality of of other instruments PCS AND TIENTS
Sensitivit TSS GSS SSS obreviations CS rvey, total score ABLE Me Key O Re IGURI 2 PCS	Moderate Severe ty to Change: I -12.70 (14.93) -3.83 (5.98) -4.07 (5.64) Cores shown in green 3. RESULT Comes ported E 3. CORRI SAMONG T	is population; I indicate strong SFR Onlin quest burde	12 11 ange (SD) CC: interclass correlationships be OM TOU e cross-settionnaire, ben of SM Mean T 50 ON BET 50	47.8 (19.6) 29.4 (11.4) in biweekly tion coefficient; CI: confi etween ISM-SAF scores CHSTONI Sectional s which in patients in SS NEEN TS SM PATIE	7.6 (6 5.0 (3 scores fi idence interval ; and measures E SM F Survey cluded n real-v S AND S AND S AND S AND S S AND	5.5) 1 5.3) 1 rom basel rom basel C1D15: cycle 1, da of other instrument PATIEN Of patie the full world se Mean (S SF-	4.2 (5.7) 0.4 (7.7) ine to C4D1 ay 15; SD: standard dev ay 15; SD: standard dev s, conversely, scores of T SURVE onts self-r ISM-SAF of 5D) SF-12 44 (1.8) FIGURE SF-12 MO 60 40 50 40 50 40 50 40 50 40	33 34 Not feas itation; PGIS: Pat shown in red indic Y (MES eportin evalua MCS 3. COR	24.8 (43.9 (ible; one iant global imp ated di SA 202 SA 202 SA 202	8.7) 13.4) e round of ression of severif 3)relationships be 20) diagno isease M TION I OUCH	4.7 (3.5) 8.8 (4.2) 14-day use (4.7 (3.5) 8.8 (4.2) 14-day use (4.7 (3.5) (4.7) (4.7) (5.7) (4.7) (4.7) (5.7) (4.7) (5.7	8.1 11. of tool	(5.3) 7 (3.9) 7 (3.9) ocytosis Quality of I of other instruments PCS AND TIENTS
ensitivit TSS GSS SSS breviations CS vey, total score ABLE Me Key O Re IGURI 20	Moderate Severe ty to Change: I -12.70 (14.93) -3.83 (5.98) -4.07 (5.64) Cores shown in green 3. RESULT Comes ported E 3. CORRI SAMONG T	is population; I indicate strong SFR Onlin quest burde	12 11 ange (SD) CC: interclass correlationships be OM TOU e cross-settionnaire, ben of SM Mean T 50 ON BET 50	47.8 (19.6) 29.4 (11.4) in biweekly tion coefficient; CI: confi etween ISM-SAF scores CHSTONI Sectional s which in patients in SS NEEN TS SM PATIE	7.6 (6 5.0 (3 scores fi idence interval ; and measures E SM F Survey cluded n real-v S AND S AND S AND S AND S S AND	5.5) 1 5.3) 1 rom basel rom basel C1D15: cycle 1, da of other instrument PATIEN Of patie the full world se Mean (S SF-	4.2 (5.7) 0.4 (7.7) ine to C4D1 ay 15; SD: standard dev ay 15; SD: standard dev s, conversely, scores of T SURVE onts self-r ISM-SAF of 5D) SF-12 44 (1.8) FIGURE SF-12 MO 60 40 50 40 50 40 50 40 50 40	33 34 Not feas itation; PGIS: Pat shown in red indic Y (MES eportin evalua MCS 3. COR	24.8 (43.9 (ible; one iant global imp ated di SA 202 SA 202 SA 202	8.7) 13.4) e round of ression of severif 3)relationships be 20) diagno isease M TION I OUCH	4.7 (3.5) 8.8 (4.2) 14-day use (4.7 (3.5) 8.8 (4.2) 14-day use (4.7 (3.5) (4.7) (4.7) (5.7) (4.7) (4.7) (5.7) (4.7) (5.7	8.1 11. of tool	(5.3) 7 (3.9) 7 (3.9) cocytosis Quality of of other instruments PCS AND IENTS

	PIONEER PAP				SERVATIONA					
Study			art 1 ⁺ (Padilla	a 2021)		Observa	tional Study (Sh	ields 2019)		
	seline Scores on I					N I I				
TSS GSS		54.2 10.9		Not reported						
SS		16.2								
Reliability	y: Internal Consist		's Alpha)			1				
-	lation	Baseline (n=38) CS-AP (n=103)								
 T	TSS 0.86				0.88					
	GSS 0.80				0.78					
	SSS	0.82								
-			bility, ICC (95% CI)							
Popula	ation		eline and C1D	015 (n=16	S Stable Participants (n=61)					
		n=17 for SSS)							
	TSS GSS	0.956 0.858				0.962 (0.936-0.977) 0.936 (0.894-0.962)				
S	SSS	0.981				· ·	937-0.977)			
Validity: S	Spearman correlat	tions of ISM-SA	total and do	main sco	res with other mea	isures (≥0.	.6=green, <0.3= <mark>r</mark>	ed)*		
Popula	ation		At time	C4D1 (n=	34)		CS	-AP (n=103)		
Concu	rrent Measure	TSS	GSS	S	SS	TSS GSS			SSS	
	SF-12 PCS	-0.226	-0.275).179	-0.631 -0.493			-0.308	
S	SF-12 MCS	-0.536	-0.368	-C).218				-0.346	
	MC-QoL	0.695	0.538		.550	0.849	0.679		0.587	
	PGIS Known-Groups an	0.656	0.401		.618 oros based on PGI	0.618	0.454		0.446	
-	-	aiysis of 15141-54			ores based on PGI	3, IVIC-Q0				
Popula				C4D1 (n=3	,			-AP (n=103)		
	Group	n	TSS mean (SD)	GSS me (SD)	ean SSS mean (SD)	n	TSS mean (SD)	GSS mean (SD)	SSS mean (SD)	
	Absent/Minimal	12	27.1 (10.2)	4.3 (3.3)		41	18.5 (14.1)	3.9 (5.1)	4.7(3.9)	
PGIS	Moderate	11	50.4 (12.1)	9.5 (2.9)		43	32.4 (13.0)	5.8 (3.7)	10.3 (5.3)	
	Severe/Very Seve		55.2 (15.1)	9.7 (6.5)		18	50.4 (20.7)	9.3 (7.7)	11.8 (5.7)	
	Mild	10	29.5 (10.6)	. ,		37	. ,	. ,		
MC-QoL			X 7	4.7 (3.6)		37	16.6 (9.9)	3.4 (3.0)	5.4 (4.7)	
	Moderate	12	43.4 (16.4)	7.3 (3.7)			29.5 (9.3)	5.1 (3.3)	9.5 (5.4)	
	Severe		55.8 (14.8)	10.7 (5.8	, , ,	33	42.0 (12.0)	8.3 (3.6)		
	Mild	11	53.4 (10.8)			34	17.2 (11.5)	3.1 (2.6)	5.6 (4.4)	
SF-12	Moderate		47.8 (19.6)	7.6 (6.5)		33	24.8 (8.7)	4.7 (3.5)	8.1 (5.3)	
a	Severe	I I	29.4 (11.4)	5.0 (3.3)		34	43.9 (13.4)	8.8 (4.2)	11.7 (3.9)	
	1	n change (SD)	n diweekiy so	cores tron	n baseline to C4D1	1				
TSS GSS	-12.70 (14.93) -3.83 (5.98)					Not feasi	ble; one round of	14-day use c	of tool	
SSS	-4.07 (5.64)									
					15: cycle 1, day 15; SD: standard de ner instruments, conversely, scores				; MC-QoL: Mastocytosis Quality of Life	
	-									
IADLE	3. RESULIS		, I STONE	SIVI PA	TIENT SURVE		DA 2020)			
					f patients self-r	-				
Me	· · · · · · · · · · · · · · · · · · ·				ne full ISM-SAF	, evalua	ted disease a	and health	icare system	
	bu	rden of SM p	patients in	real-wo	orld settings.					
Key O	outcomes	Mean TS	S	Μ	ean (SD) SF-12	MCS	M	ean (SD)	SF-12 PCS	
Rej	ported	50			44 (1.8)			43 (2	2.5)	
								(-	/	
FIGURE	E 3. CORREL	ATION BETW	/EEN TSS	AND S	F- FIGURE	3. COR	RELATION E	BETWEEN	NTSS AND	
	AMONG TOU					CS AMO	ONG TOUCH	STONE S		
	TSS & SF-12 PCS1 Correlation						TSS & SF-12 MCS1	Correlation		
70					60		•			
60	•				50	•	•	•		
**************************************	•	•				**************************************	••			
50	·····	• •			40	·····		•		
တ္လ 40	*****	•			Ň			••••••	•	
-12 PC		······································	•		27 30		•	•	·····	
й			•		– Š	•	•	• •	•	
20	•		••••••	R ² = 0.4	20		• •	•	R ² = 0.14	
20		•	•							
10	TSS >28 TSS ≤28	•	•		10					
0 0	20 40	60	80	100	120 0 0	20	40 60	80	100 120	
		Fotal Symptom Score (TSS)					Total Symptom So	core (TSS)		
		•	•		rent scoring systems for SF-12 a					



§ Negative correlation is expected due to different scoring systems for SF-12 and ISM-SAF Disclosures: This study was funded by Blueprint Medicines Corporation (BPMC). BPMC participated in the interpretation of data, review, and approval of the publication. ES and MR are employees of BPMC.

DITY, AND SENSITIVITY RESULTS
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