Urinary Mast Cell Metabolites Versus Serum Tryptase for Monitoring Response to Cytoreductive Therapy in Indolent Systemic Mastocytosis: A Multi-Site Mayo Clinic Analysis

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BACKGROUND

- Systemic mastocytosis (**SM**) is a clonal mast cell neoplasm driven by KIT D816V mutation (>90% of cases).
- Indolent SM (ISM) is the most common subtype, carries near-normal life expectancy but significant mediator-related symptoms, and is the primary target of selective KIT inhibitors.
- Serum tryptase is the standard monitoring biomarker but often normalizes early on selective KIT inhibitors, even when symptoms persist.
- Urinary mast cell metabolites [N-methylhistamine (**NMH**), prostaglandin D_2 metabolite (**2,3-dinor-11β-PGF2α**), and leukotriene E_4 (**LTE_4**)] may offer complementary activation monitoring, but data during cytoreductive therapy (**CRT**) are limited.

OBJECTIVE

- Evaluate the comparative utility of serum tryptase versus urinary mast cell metabolites as biomarkers of clinical response to CRT in ISM.

METHODS

- **Study Design**: Retrospective, multi-site analysis of ISM patients receiving CRT at three Mayo Clinic sites (AZ, FL, MN) during 2020–2025).
- **Inclusion Criteria**: ISM diagnosis, CRT use, and paired pre- and post-treatment serum tryptase and urinary metabolite measurements.
- **Exclusion Criteria**: Advanced SM subtypes, missing paired biomarker data.
- **Clinical Response**: Defined as patient-reported improvement in ≥1 mastocytosis symptom domain (e.g., dermatologic, gastrointestinal, cardiovascular, musculoskeletal, neuropsychiatric).
- **Statistical Analysis**: Associations between percent biomarker change (reduction or increase) and clinical response were assessed using Spearman correlation.

RESULTS

Table 1. Baseline Patient Characteristics

Patients Cohort	
SM patients screened across Mayo Clinic sites	608
Patients meeting inclusion criteria	29
Demographics	
Female	23 (79%)
Male	6 (21%)
Median age (range), years	60 (44-76)
Mayo Clinic Site	
Minnesota	16 (55%)
Arizona	13 (45%)
Florida	0 (0%)
Treatment	
Avapritinib	27 (93%)
Bezuclastinib	2 (7%)
Overall Clinical Response	
Substantial improvement	12 (41%)
Moderate improvement	15 (59%)
Mild improvement	2 (6%)
Common Baseline Symptoms	
Flushing	19 (66%)
Fatigue	17 (59%)
Rash/pruritus	17 (59%)
Gastrointestinal symptoms	15 (52%)
Headache	10 (34%)

Table 2. Spearman Correlation Between Biomarker Reduction and Clinical Response

Biomarker	r	p-value
Serum Tryptase	0.654	<0.001
NMH	0.532	<0.003
2,3-dinor-11β-PGF2α	−0.104	0.629
LTE_4	−0.107	0.626

Figure 1. Waterfall Analysis of Biomarker Reduction Following Cytoreductive Therapy

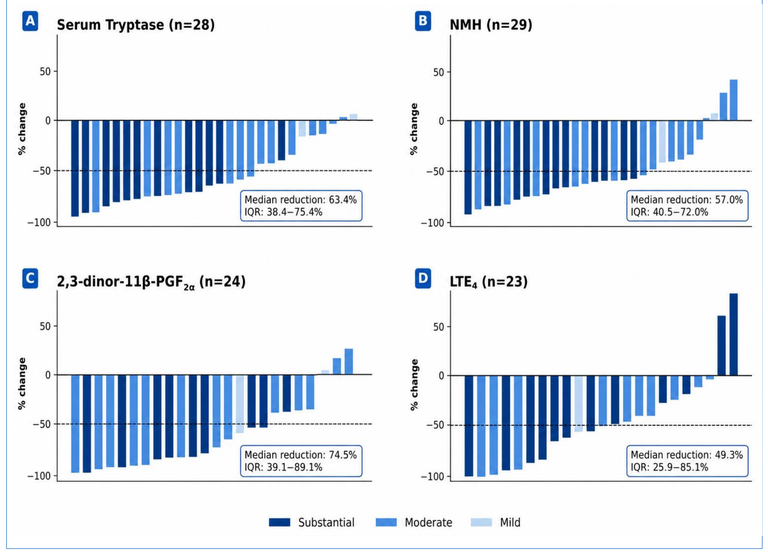
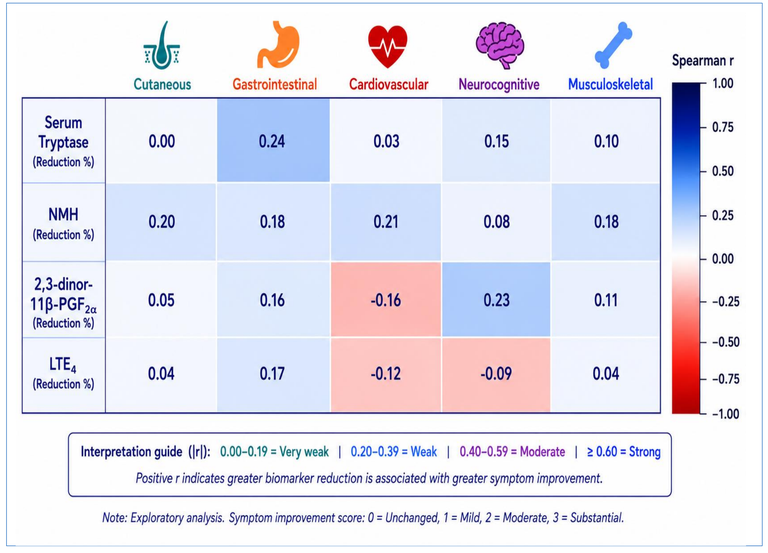


Figure 2. Heatmap Between Biomarker Reduction and Symptom Improvement



CONCLUSIONS

- **Serum tryptase** demonstrated the strongest correlation with clinical response (r=0.654, p<0.001) and should remain the primary biomarker for monitoring cytoreductive therapy in ISM.
- **NMH** also correlated significantly with clinical improvement (r=0.532, p=0.003), supporting its role as a complementary adjunctive biomarker.
- **2,3-dinor-11β-PGF2α and LTE_4** reductions were variable and showed no association with symptoms improvement, suggesting limited utility for treatment monitoring (excluding patients on aspirin did not alter the lack of correlation observed with **2,3-dinor-11β-PGF2α**).
- Clinical improvement was observed across multiple symptom domains, with the **greatest responses seen in cutaneous and gastrointestinal symptoms**, while musculoskeletal and neurocognitive improvement was more variable.

LIMITATIONS

- Small sample size, retrospective design, and predominantly avapritinib-treated cohort limit statistical power and generalizability.
- Larger, prospective studies with serial biomarker assessments and routine validated patient-reported outcome measures are needed to define the optimal biomarker panel for CRT monitoring in ISM.

REFERENCES

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CONTACT INFORMATION

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