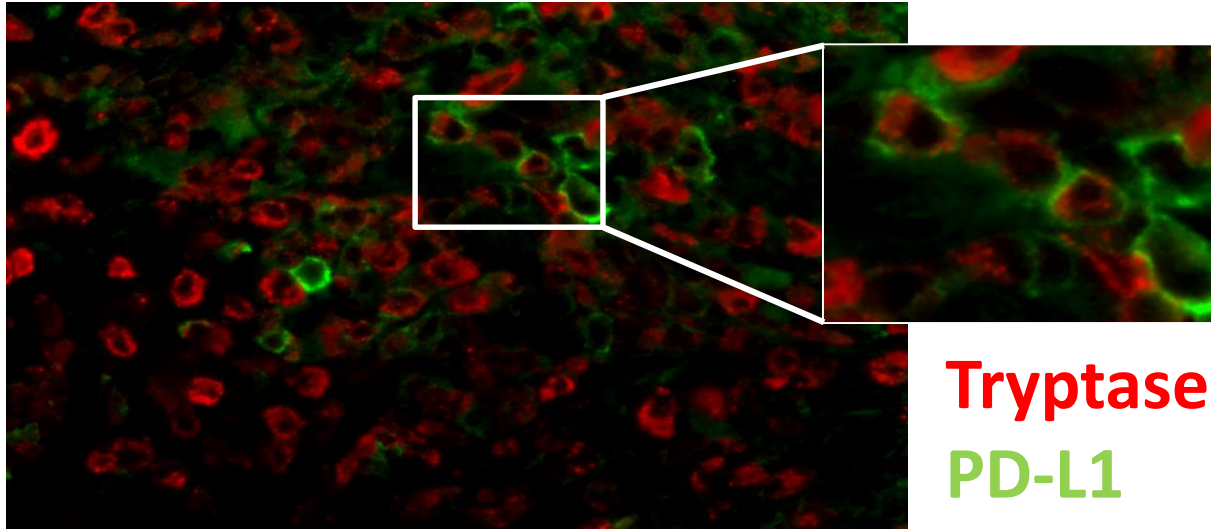


# Updates in Mastocytosis



**Tryptase**  
**PD-L1**

**Tracy I. George, M.D.**  
Professor of Pathology



**HEALTH**  
UNIVERSITY OF UTAH



# Disclosure: *Tracy George, M.D.*

---

Research Support / Grants

None

Stock/Equity (any amount)

None

Consulting

Blueprint Medicines

Novartis

Employment

ARUP Laboratories

Speakers Bureau / Honoraria

None

Other

None

# Outline

- Classification
- Advanced mastocytosis
- A case report
- Clinical trials
- Other potential therapies

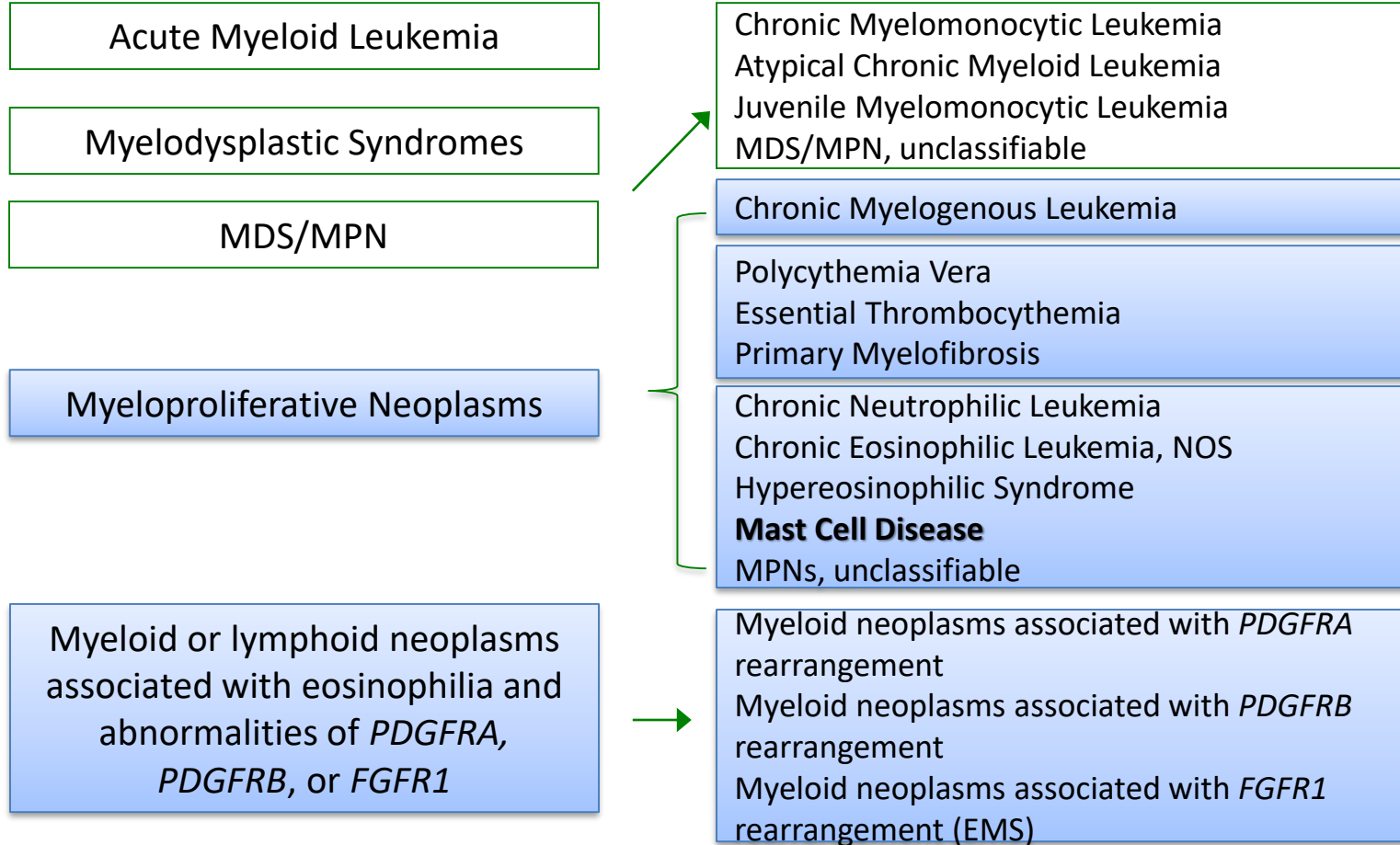
# Outline

- **Classification**
- Advanced mastocytosis
- A case report
- Clinical trials
- Other potential therapies

***Mastocytosis symposium and consensus meeting on  
classification and diagnostic criteria for mastocytosis***  
**Boston, October 25-28, 2012**



# 2008 WHO Classification Scheme for Myeloid Neoplasms



# 2017 WHO Classification Scheme for Myeloid Neoplasms

Acute Myeloid Leukemia

Myelodysplastic Syndromes

MDS/MPN

Myeloproliferative Neoplasms

**Mastocytosis**

Myeloid/ lymphoid neoplasms  
with eosinophilia and gene  
rearrangement

Chronic Myelomonocytic Leukemia  
Atypical Chronic Myeloid Leukemia  
Juvenile Myelomonocytic Leukemia  
MDS/MPN with ring sideroblasts and thrombocytosis  
MDS/MPN, unclassifiable

Chronic Myeloid Leukemia

Polycythemia Vera  
Essential Thrombocythemia  
Primary Myelofibrosis

Chronic Neutrophilic Leukemia  
Chronic Eosinophilic Leukemia, NOS  
MPN, unclassifiable

Myeloid/lymphoid neoplasms with *PDGFRA*  
rearrangement  
Myeloid/lymphoid neoplasms with *PDGFRB*  
rearrangement  
Myeloid/lymphoid neoplasms with *FGFR1*  
rearrangement  
Myeloid/lymphoid neoplasms with *PCM1-JAK2*

# WHO 2008 definition of systemic mastocytosis

---

*Major:* Multifocal dense infiltrates of mast cells

*Minor:*

- >25% of mast cells with atypical morphology
- D816V *KIT* mutation
- CD25 and/or CD2
- Serum total tryptase >20 ng/mL  
(unless associated myeloid disorder)

Morgado JM, Sánchez-Muñoz L, Teodósio CG, Jara-Acevedo M, Alvarez-Twose I, Matito A, Fernández-Nuñez E, García-Montero A, Orfao A, Escribano L. Immunophenotyping in systemic mastocytosis diagnosis: 'CD25 positive' alone is more informative than the 'CD25 and/or CD2' WHO criterion. *Mod Pathol.* 2012;25:516-21.



# WHO 2008 definition of systemic mastocytosis

---

*Major:* Multifocal dense infiltrates of mast cells

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- D816V *KIT* mutation
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Morgado JM, Sánchez-Muñoz L, Teodósio CG, Jara-Acevedo M, Alvarez-Twose I, Matito A, Fernández-Nuñez E, García-Montero A, Orfao A, Escribano L. Immunophenotyping in systemic mastocytosis diagnosis: 'CD25 positive' alone is more informative than the 'CD25 and/or CD2' WHO criterion. *Mod Pathol.* 2012;25:516-21.

# WHO 2017 definition of systemic mastocytosis

---

*Major:* Multifocal dense infiltrates of mast cells

*Minor:*

- >25% of mast cells with atypical morphology
- D816V *KIT* mutation
- CD25 *with or without* CD2
- Serum total tryptase >20 ng/mL  
(unless associated myeloid disorder)

# WHO 2008 Classification of Mastocytosis

---

- Cutaneous mastocytosis
- Systemic mastocytosis
  - Indolent systemic mastocytosis
  - Systemic mastocytosis with associated clonal, hematologic non-mast cell lineage disease
  - Aggressive systemic mastocytosis
  - Mast cell leukemia
- Mast cell sarcoma
- Extracutaneous mastocytoma

# WHO 2017 Classification of Mastocytosis

---

- Cutaneous mastocytosis
- Systemic mastocytosis
  - Indolent systemic mastocytosis
  - Smoldering systemic mastocytosis ←
  - Systemic mastocytosis with *associated hematologic neoplasm*
  - Aggressive systemic mastocytosis
  - Mast cell leukemia
    - acute
    - chronic
- Mast cell sarcoma
- Extramedullary plasmacytoma

P Valent et al. Refined diagnostic criteria and classification of mast cell leukemia and myelomastocytic leukemia: a consensus proposal. *Ann Oncol* 2014;24(9):1691-1700.

# ***What is mastocytosis?***

- Clonal, neoplastic proliferation of mast cells
- Heterogeneous disorder:
  - Skin lesions that spontaneously regress to highly aggressive leukemias with short survival and multiorgan failure
- Subtypes determined by distribution and clinical manifestations



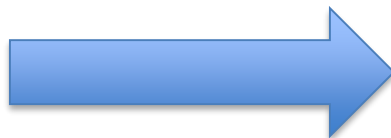
?Diagnosis

# Telangiectasia macularis eruptiva perstans (TMEP)





Adults with cutaneous mastocytosis lesions  
-Urticaria pigmentosa  
-TMEP



Systemic mastocytosis  
-most indolent  
-fewer advanced

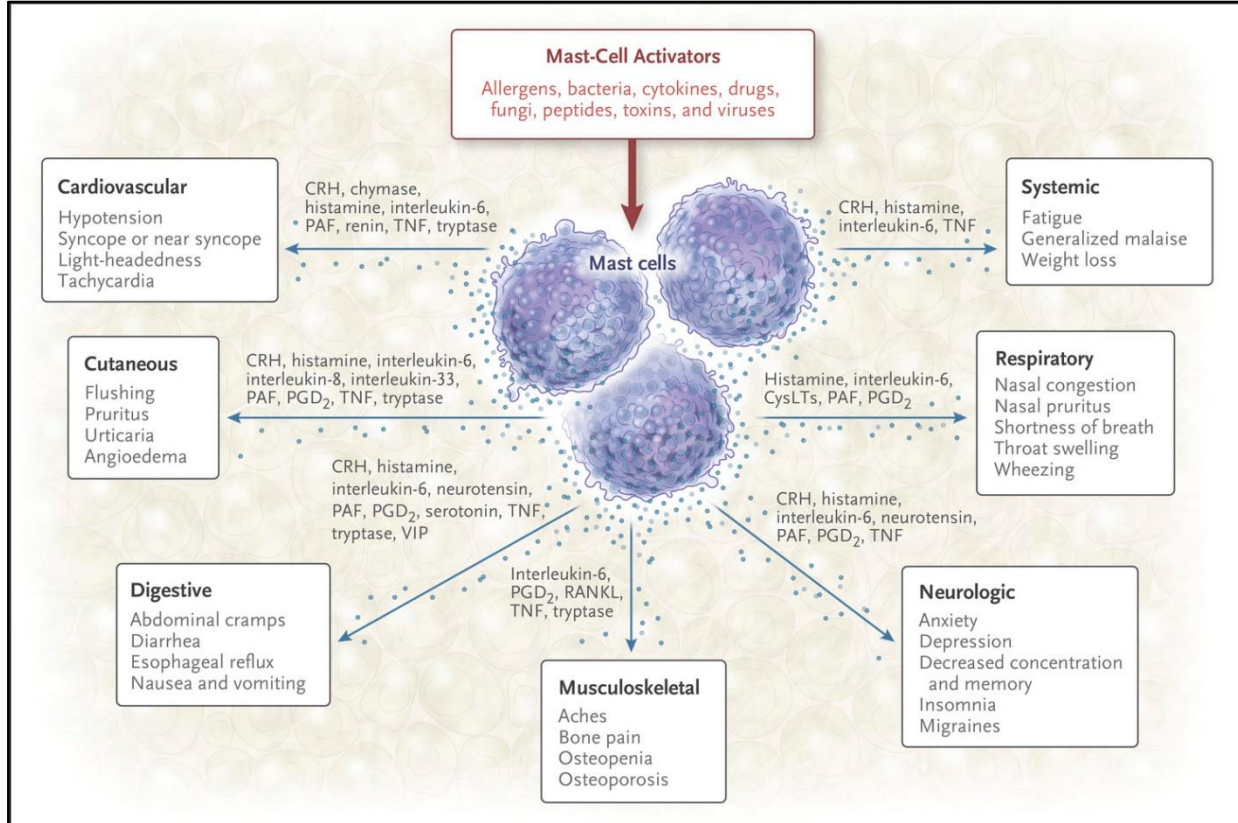


Cutaneous mastocytosis only  
-sampling error

Work up:

1. Skin biopsy
2. Serum tryptase (basal and event-related)
3. Bone marrow biopsy with appropriate ancillary studies

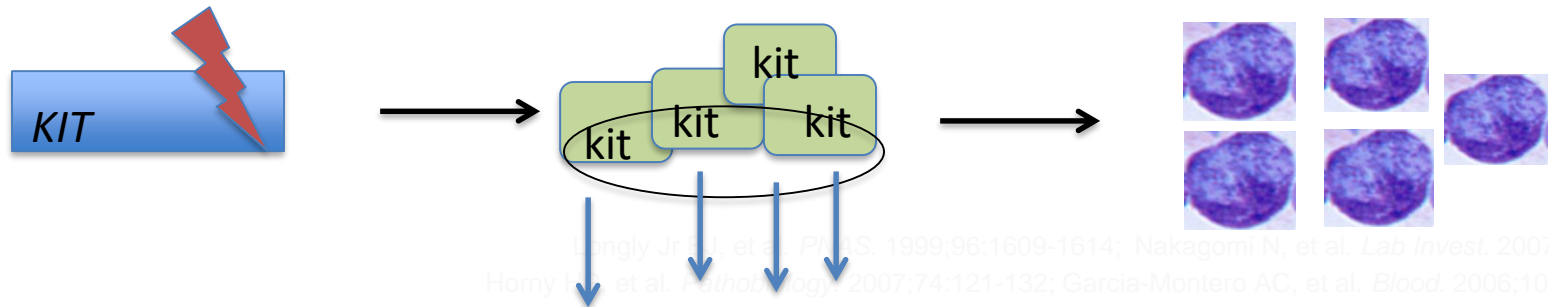
# Clinically Relevant Mediators Released from Mast Cells and Putative Effects.





# Pathogenesis of SM

- Somatic *KIT* point mutations in neoplastic mast cells
- Constitutive activation of the receptor tyrosine kinase KIT
- Induces increased mast cell proliferation and motility, resulting in infiltration of neoplastic mast cells into various organs



# Classification of Mastocytosis

---



**Cutaneous mastocytosis (CM) Systemic mastocytosis (SM)**

# Classification of Mastocytosis

---

CM

Systemic mastocytosis (SM)

Indolent SM

Smoldering SM

SM with an associated hematologic neoplasm (SM-AHN)

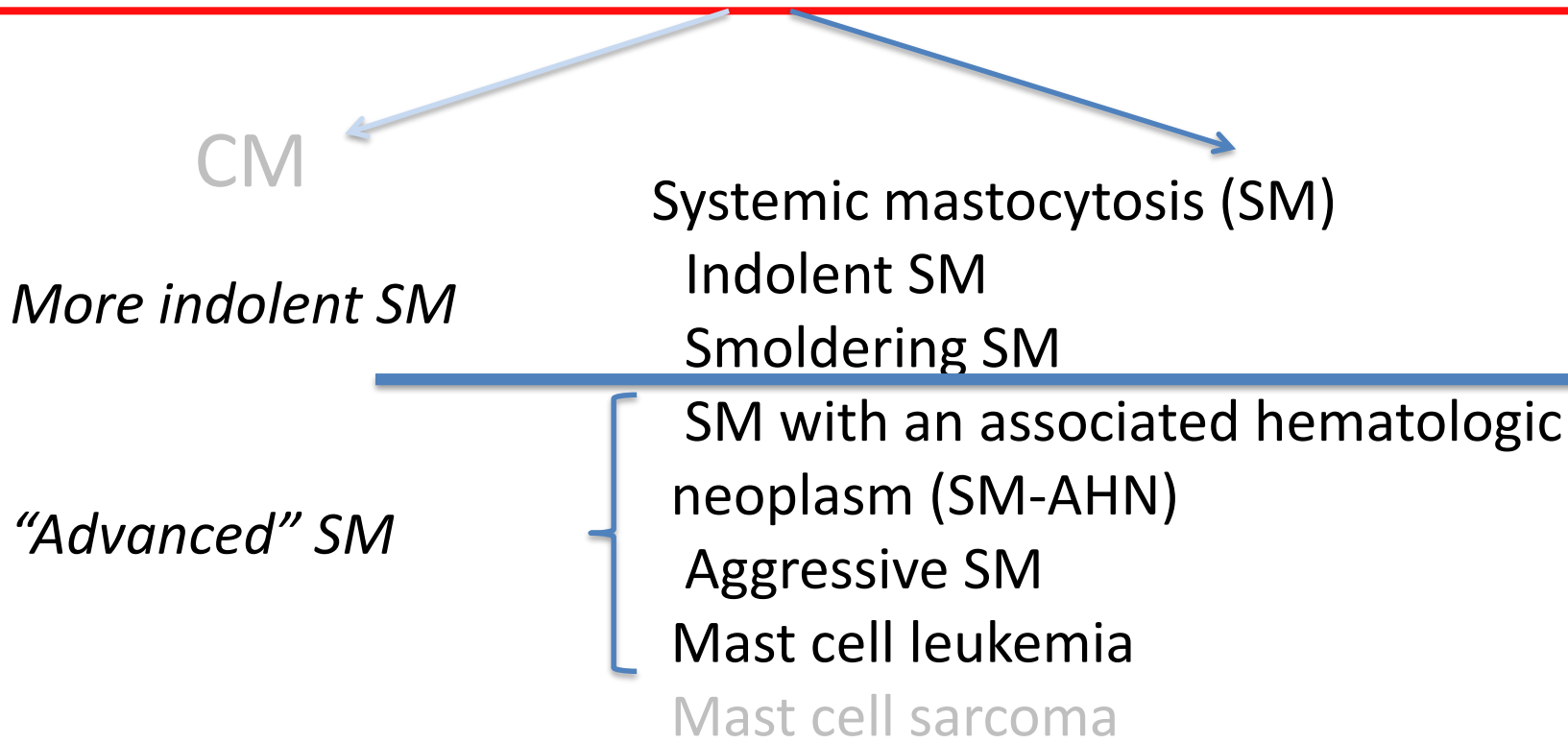
Aggressive SM

Mast cell leukemia

Mast cell sarcoma

# Classification of Mastocytosis

---



# Advanced Systemic Mastocytosis



## **ASM** (1+ "C"=cytoreductive requiring findings)

- *BM dysfunction → cytopenias*
- *Palpable hepatomegaly with impaired liver function, ascites, +/- portal hypertension*
- *Skeletal involvement → large osteolytic lesions, and/or pathological fractures*
- *Palpable splenomegaly w/ hypersplenism*
- *Malabsorption, weight loss due to GI mast cell infiltrates, hypoalbuminemia*

## **Mast cell leukemia**

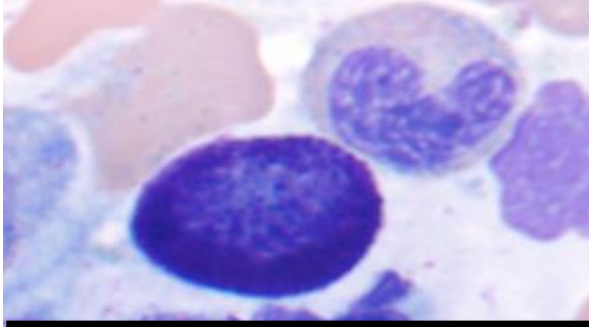
*≥20% mast cells on aspirate/PB*

## **SM + AHN**

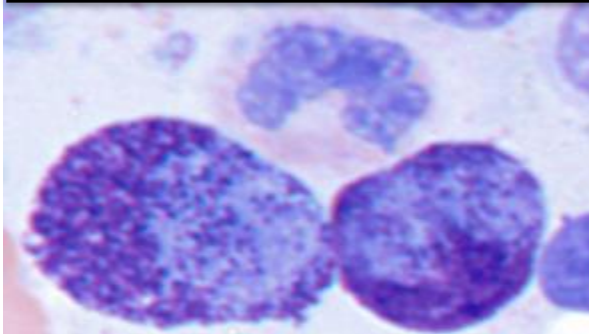
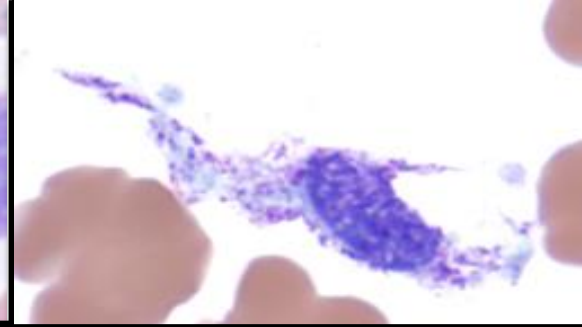
*-meet WHO criteria for an associated hematological neoplasm*  
*-meet SM criteria*

# Cytology of mast cells

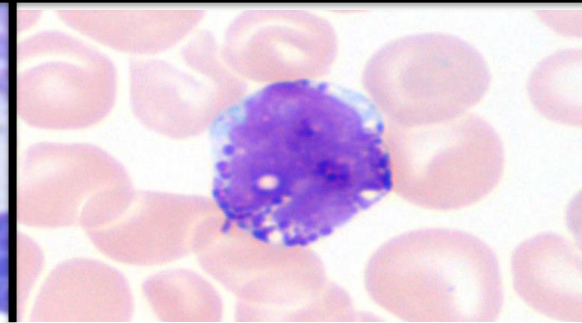
Normal/reactive/well-differentiated



Atypical type I



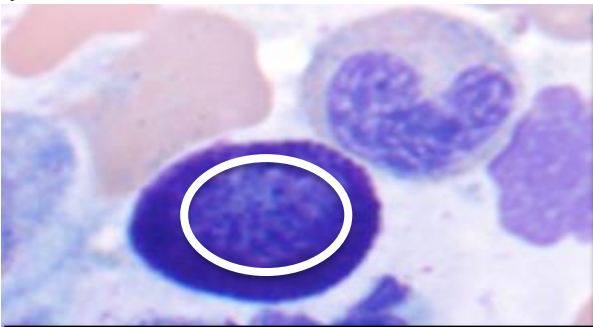
Atypical type II



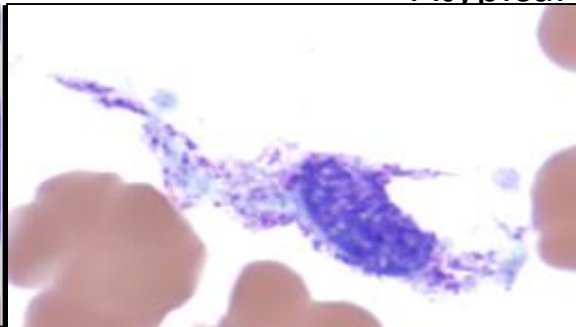
Metachromatic blast

# Cytology of mast cells

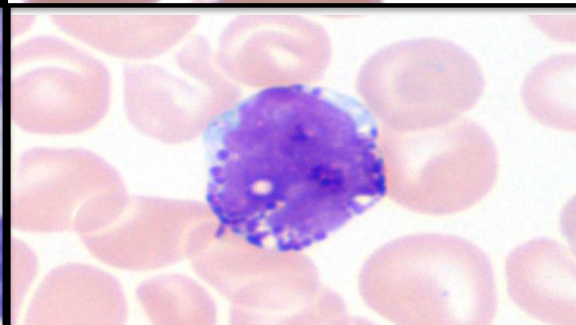
Normal/reactive/well-differentiated



Atypical type I

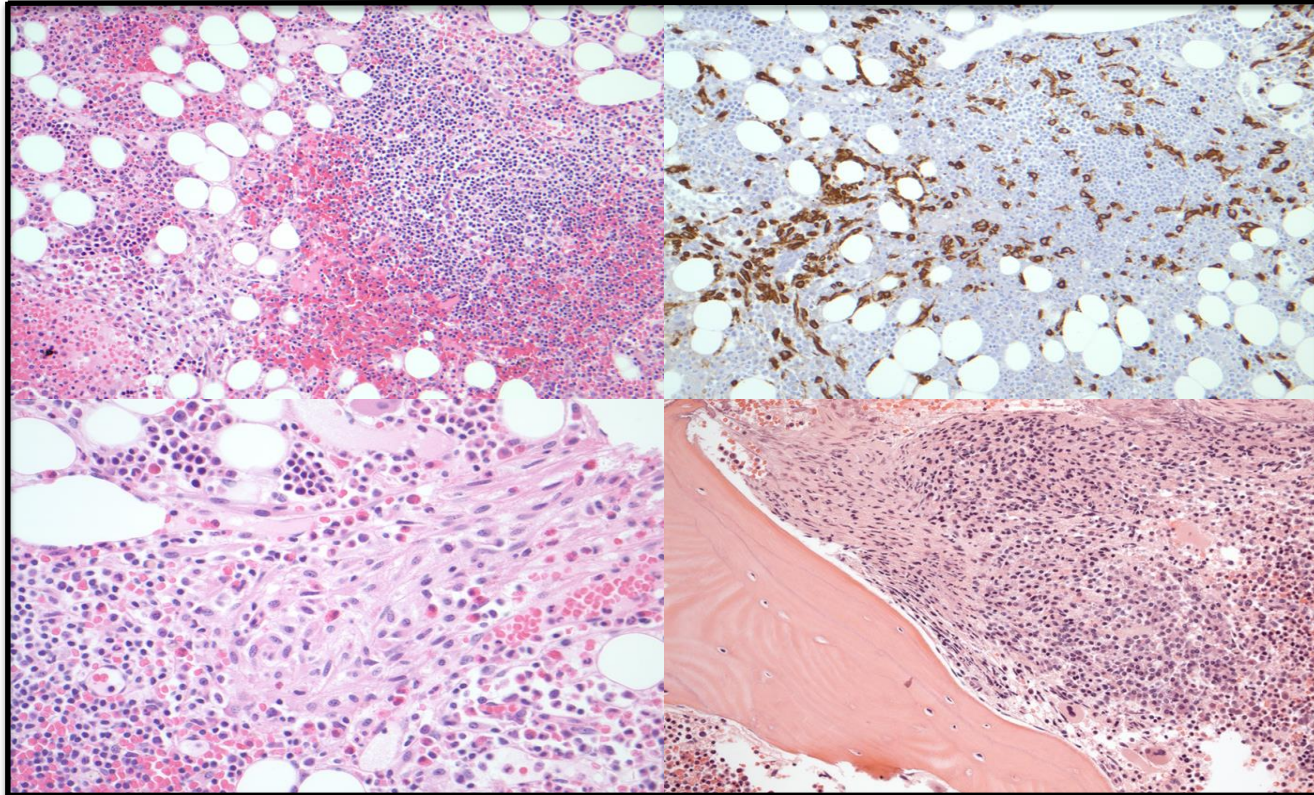


Atypical type II



Metachromatic blast

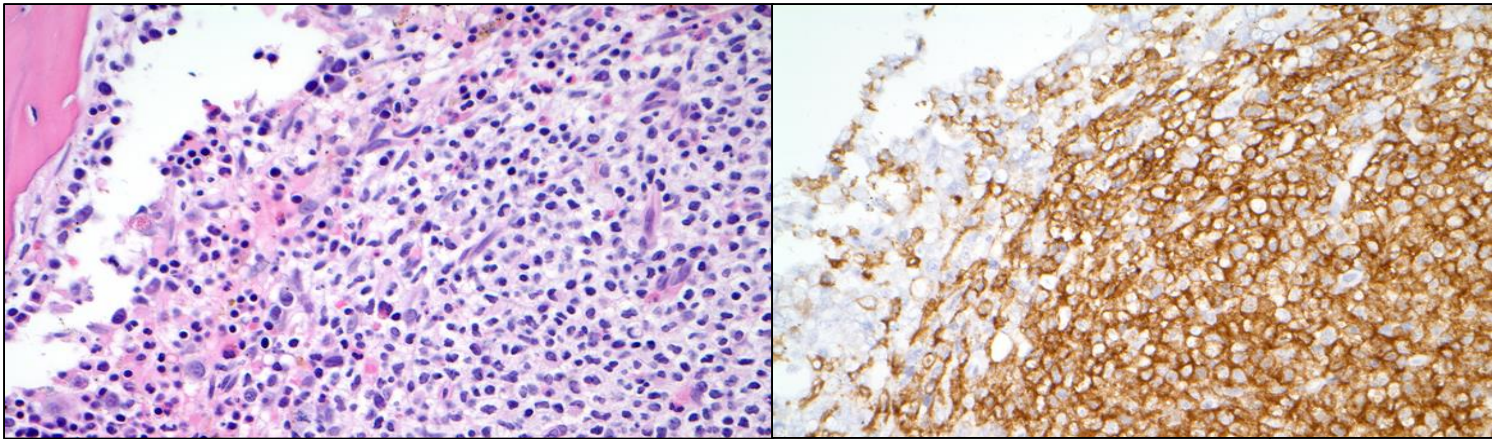
# Indolent systemic mastocytosis



tryptase

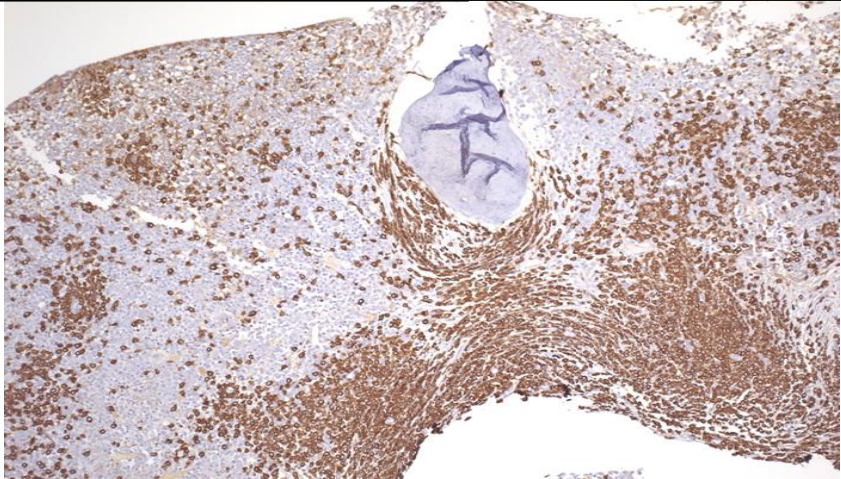


# ASM-AHN



CD117

ASM-  
MDS/MPN,U

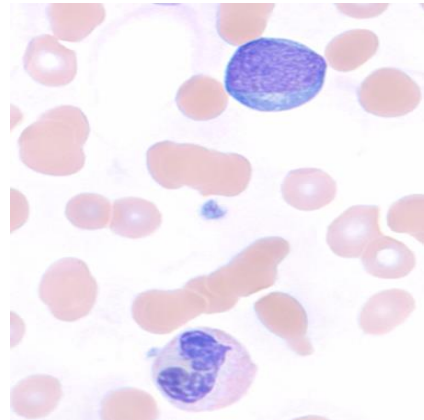
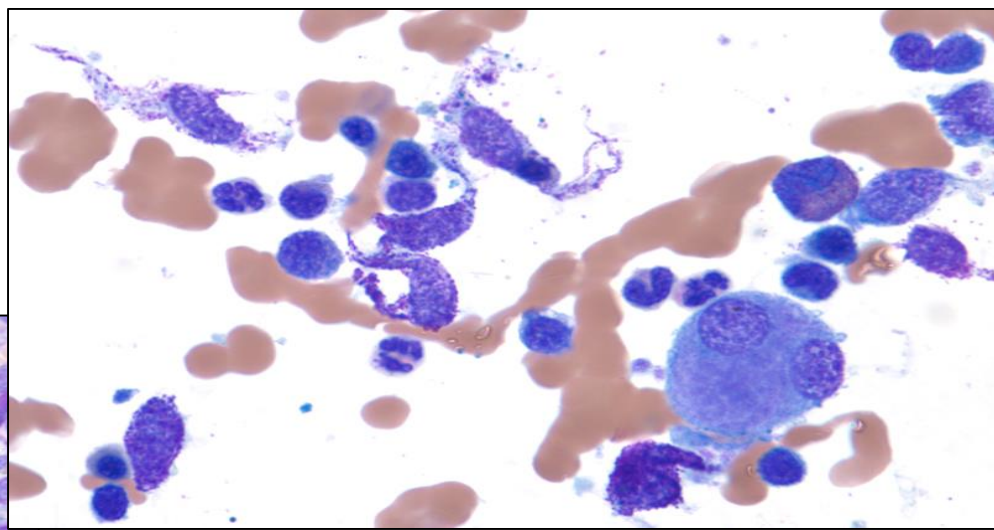
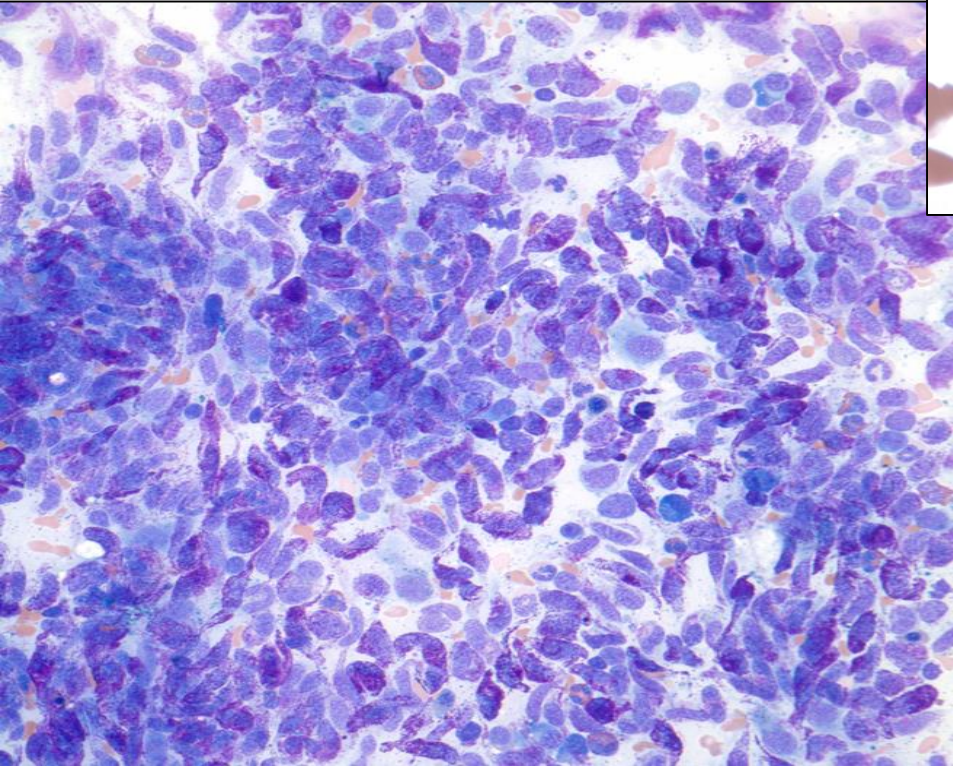


ASM-CMML

tryptase

# Mast cell leukemia

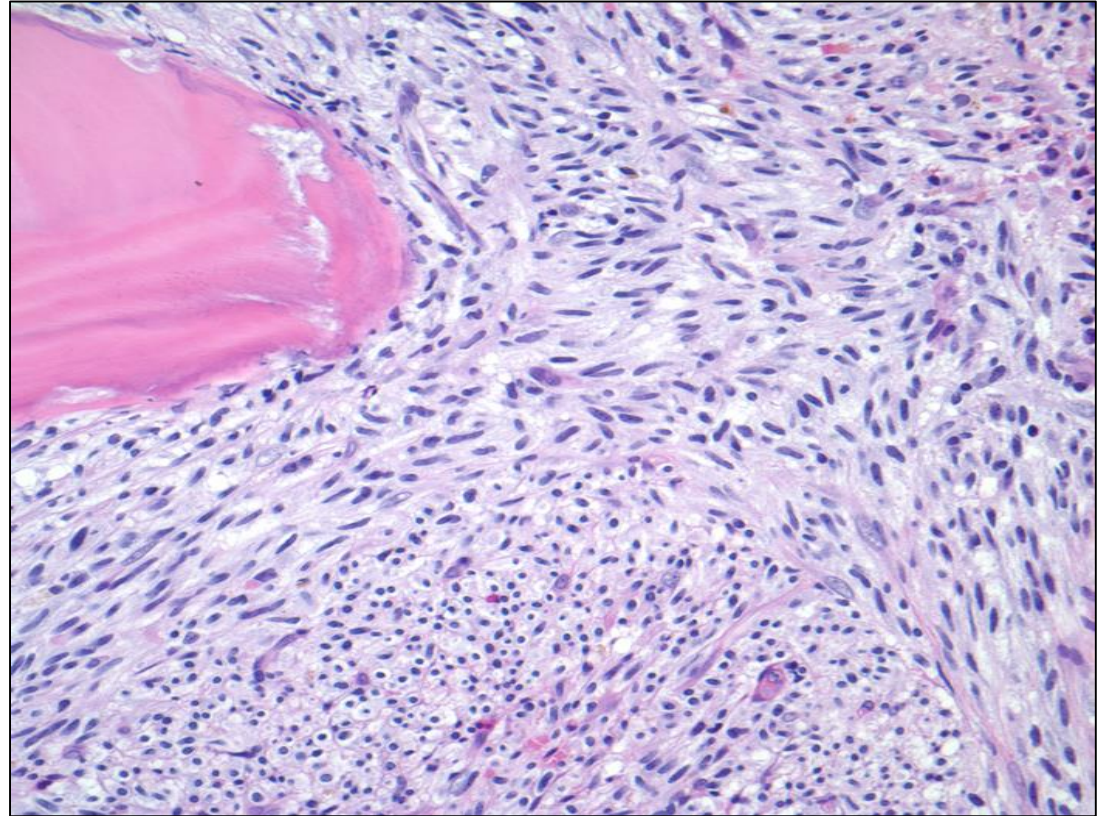
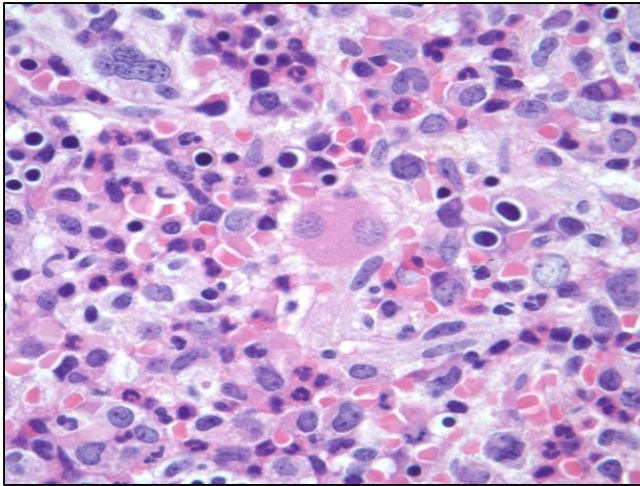
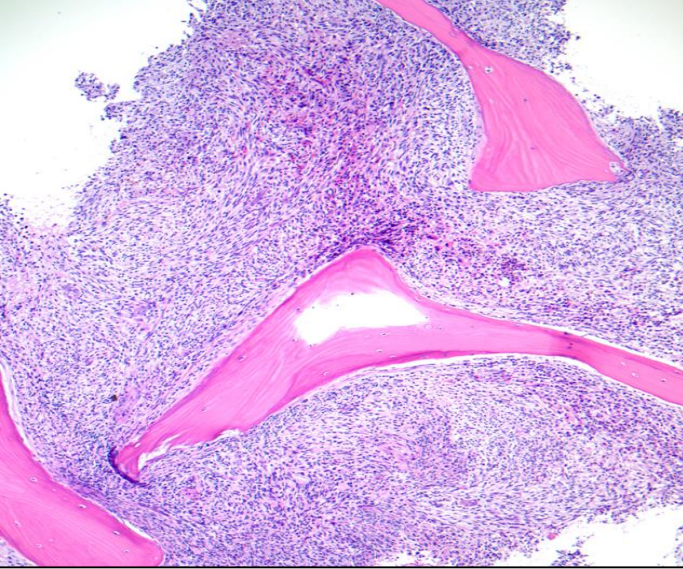
Bone marrow aspirate



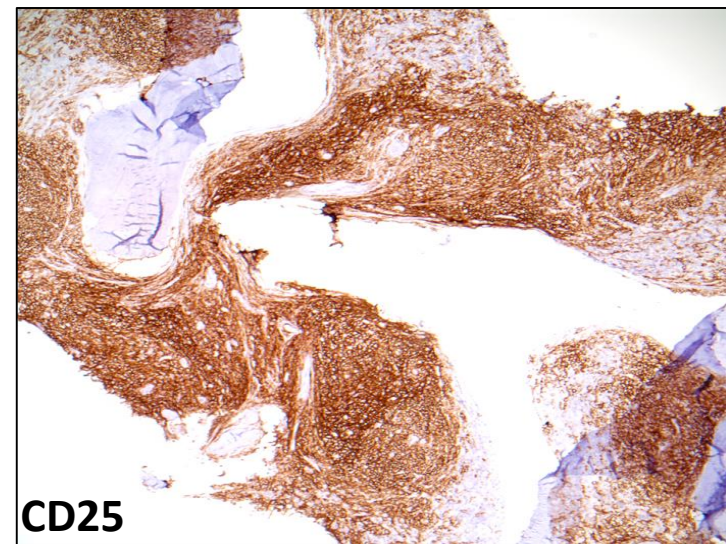
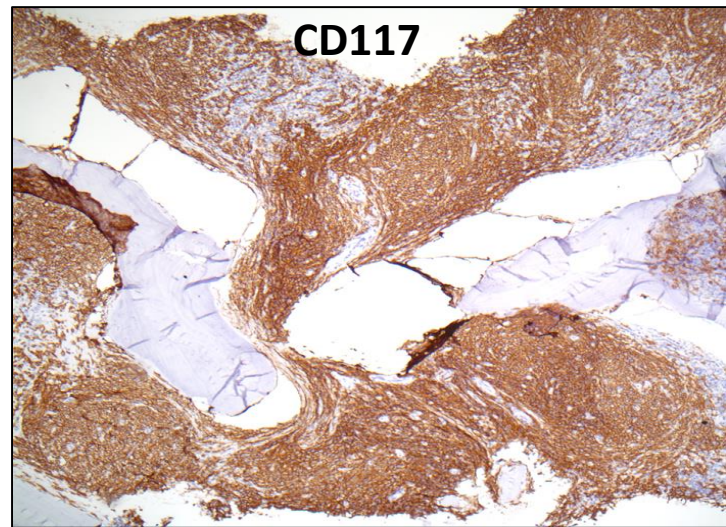
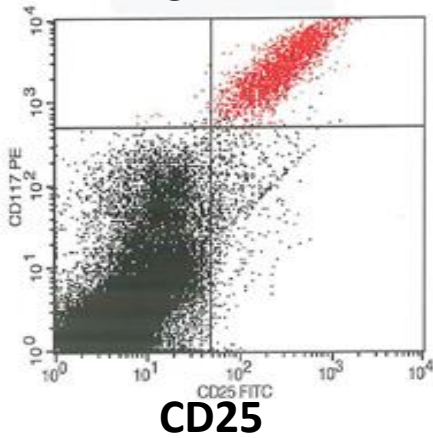
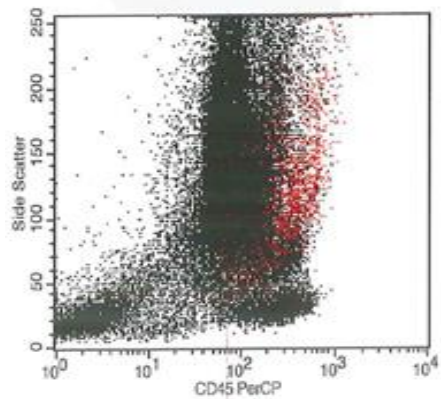
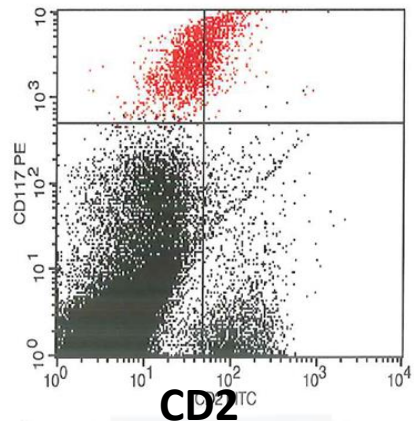
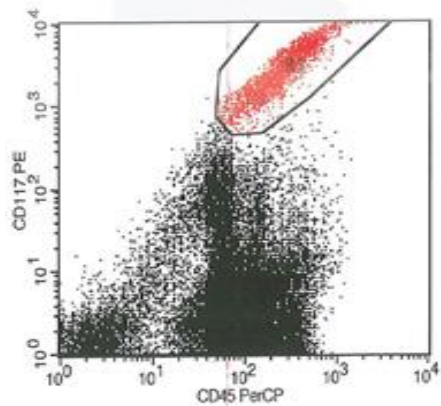
Blood smear

Laboratory values:  
Hb: 8.8 g/dL  
WBC, PLT: Normal  
Serum tryptase: 763

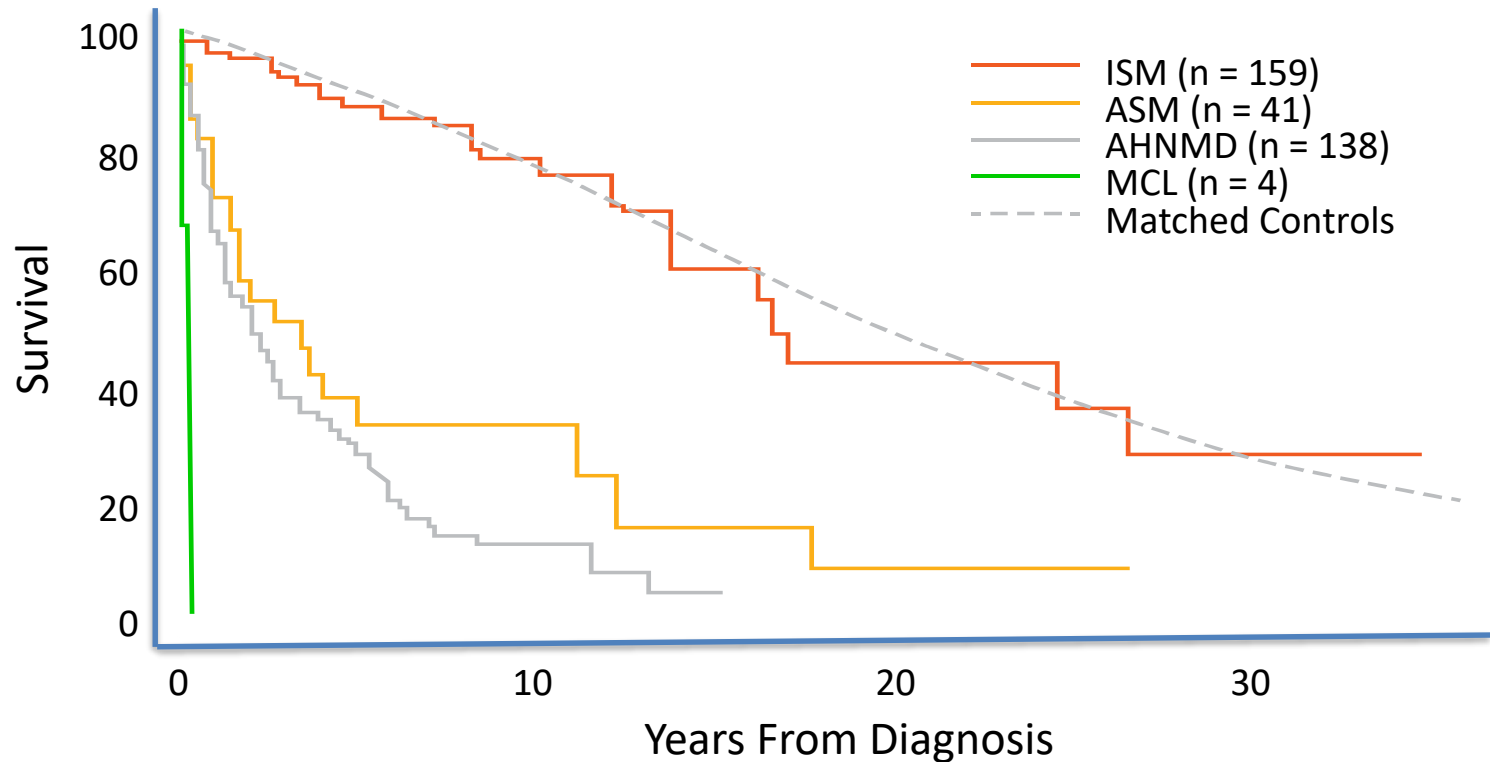
# Bone marrow biopsy



Tryptase IHC positive  
KIT D816V positive  
MAST CELL ANALYSIS

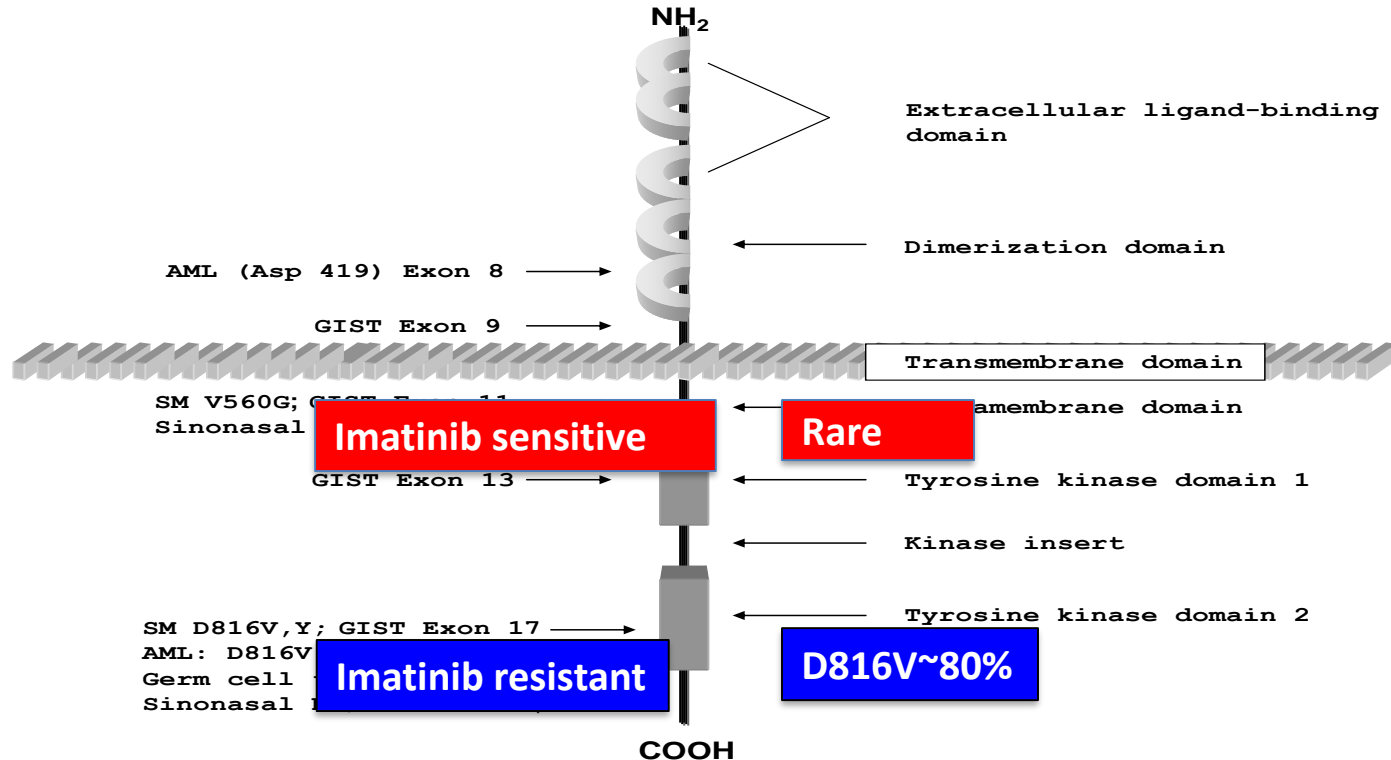


# Overall Survival



- Kaplan–Meier survival for SM patients classified by WHO disease type compared with the expected age and sex-matched US population’s survival for the entire cohort

# KIT Mutations: Implications for TK Inhibitors



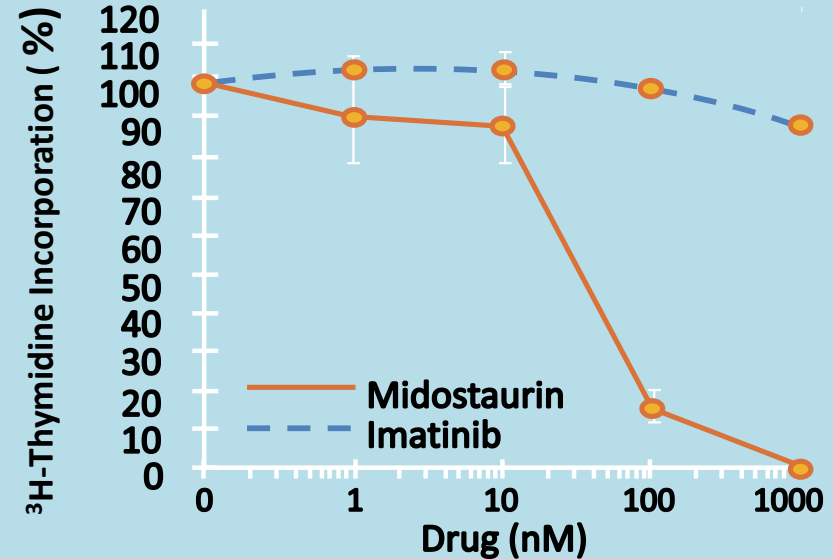
GIST: Gastrointestinal stromal tumors; SM: Systemic Mastocytosis; AML: acute myelogenous leukemia;  
NK/T-CL: Natural killer/T-cell lymphoma

# Treatment

- Challenging due to the diversity and complexity of disease and the lack of a standard and highly effective therapy
- Current therapies include:
  - Observation
  - Topical therapies for cutaneous disease
  - Symptomatic noncytoreductive therapies
  - Cytoreductive therapy
    - Indicated by the presence of organ dysfunction
    - Used to reduce mast cell burden

# Sensitivity of c-KIT D816V-Transformed Ba/F3 Cell Lines to Midostaurin and Imatinib

- Midostaurin inhibited growth of all c-KIT-transformed Ba/F3 cell lines
- Cell lines resistant to imatinib due to expression of c-KIT D816V are inhibited by midostaurin
- Results have been confirmed in additional cell lines



IC<sub>50</sub> for midostaurin: 44 nM

IC<sub>50</sub> for imatinib: > 1 μM



# Midostaurin

- Potent inhibitor of all common mutant forms of c-KIT, including D816V,D816Y
- May preferentially inhibit cells expressing mutant c-KIT compared to wild-type c-KIT
- Counteracts anti-IgE-induced release of histamine in blood basophils and cultured cord blood cell-derived mast cells
  - Effects were dose-dependent; occurred at pharmacologic concentrations

## Brief report

Activity of the tyrosine kinase inhibitor PKC412 in a patient with mast cell leukemia with the D816V *KIT* mutation

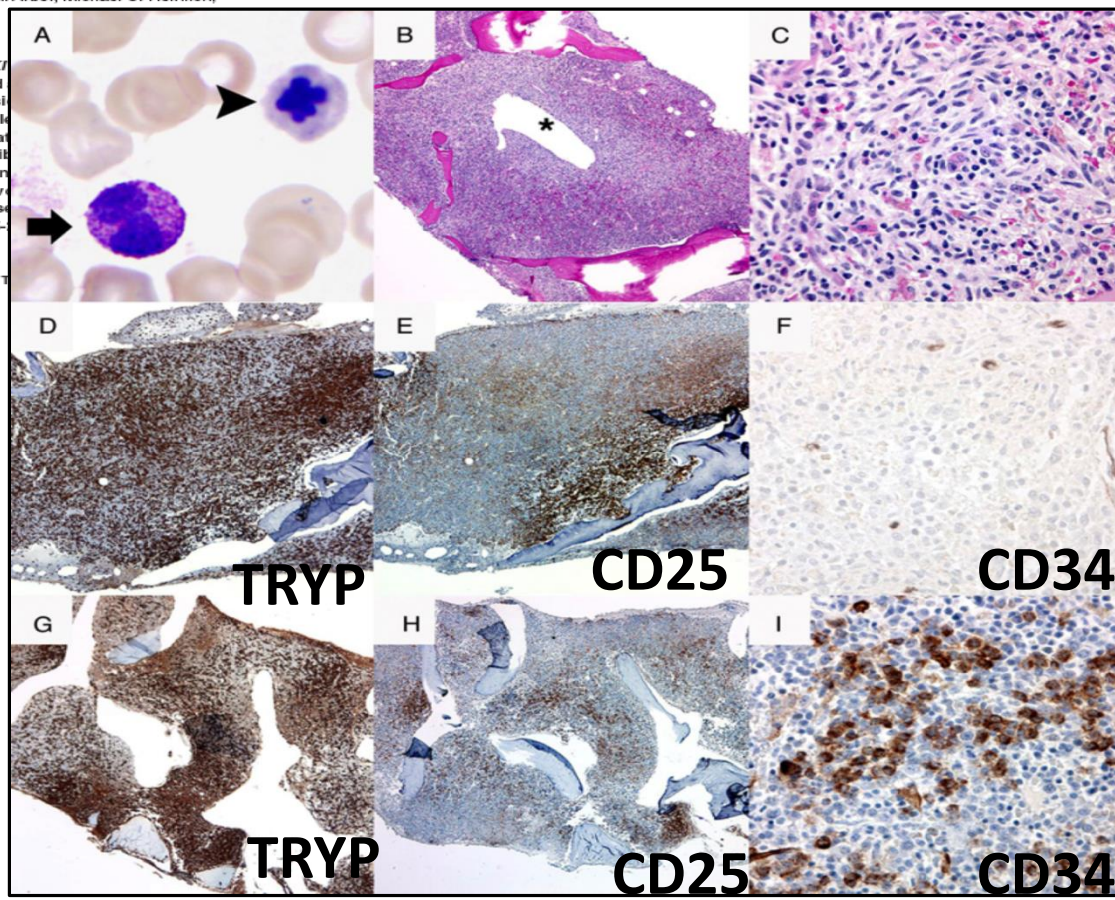
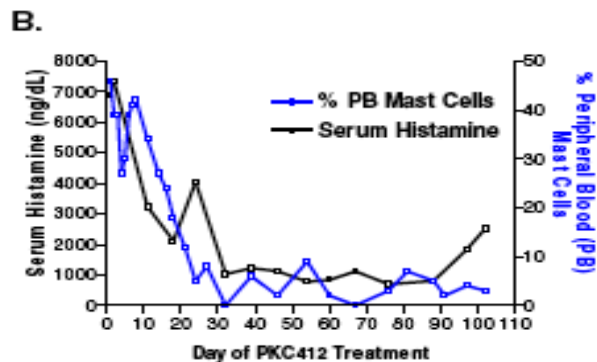
Jason Gotlib, Caroline Berubé, Joseph D. Gowney, Ching-Cheng Chen, Tracy I. George, Christopher Williams, Tomohiro Kajiguchi, Jia Ruan, Stan L. Lilleberg, Jeffrey A. Durocher, Jack H. Lichy, Yanfeng Wang, Pamela S. Cohen, Daniel A. Arber, Michael C. Heinrich, Len Neckers, Stephen J. Galli, D. Gary Gilliland, and Steven E. Coutre

The majority of patients with systemic mast cell disease express the imatinib-resistant Asp816Val (D816V) mutation in the *KIT* receptor tyrosine kinase. Limited treatment options exist for aggressive systemic mastocytosis (ASM) and mast cell leukemia (MCL). We evaluated whether PKC412, a small-molecule inhibitor of *KIT* with a different chemical structure from imatinib, may have therapeutic use in advanced SM with the D816V *KIT* mutation. We treated a patient with MCL (with an associated myelodysplastic syn-

drome (MDS)/myeloproliferative disorder [MPD]) based on in vitro studies demonstrating that PKC412 could inhibit D816V *KIT*-transformed Ba/F3 cell growth with a 50% inhibitory concentration ( $IC_{50}$ ) of 30 nM to 40 nM. The patient exhibited a partial response with significant resolution of liver function abnormalities. In addition, PKC412 treatment resulted in a significant decline in the percentage of peripheral blood mast cells and serum histamine level and was associated with a decrease in *KIT* phosphorylation and

D816V *KIT* patient died progressive myeloid leukates that is a feasible agent clinical evmic phase 106:2865-

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JOURNAL of MEDICINE

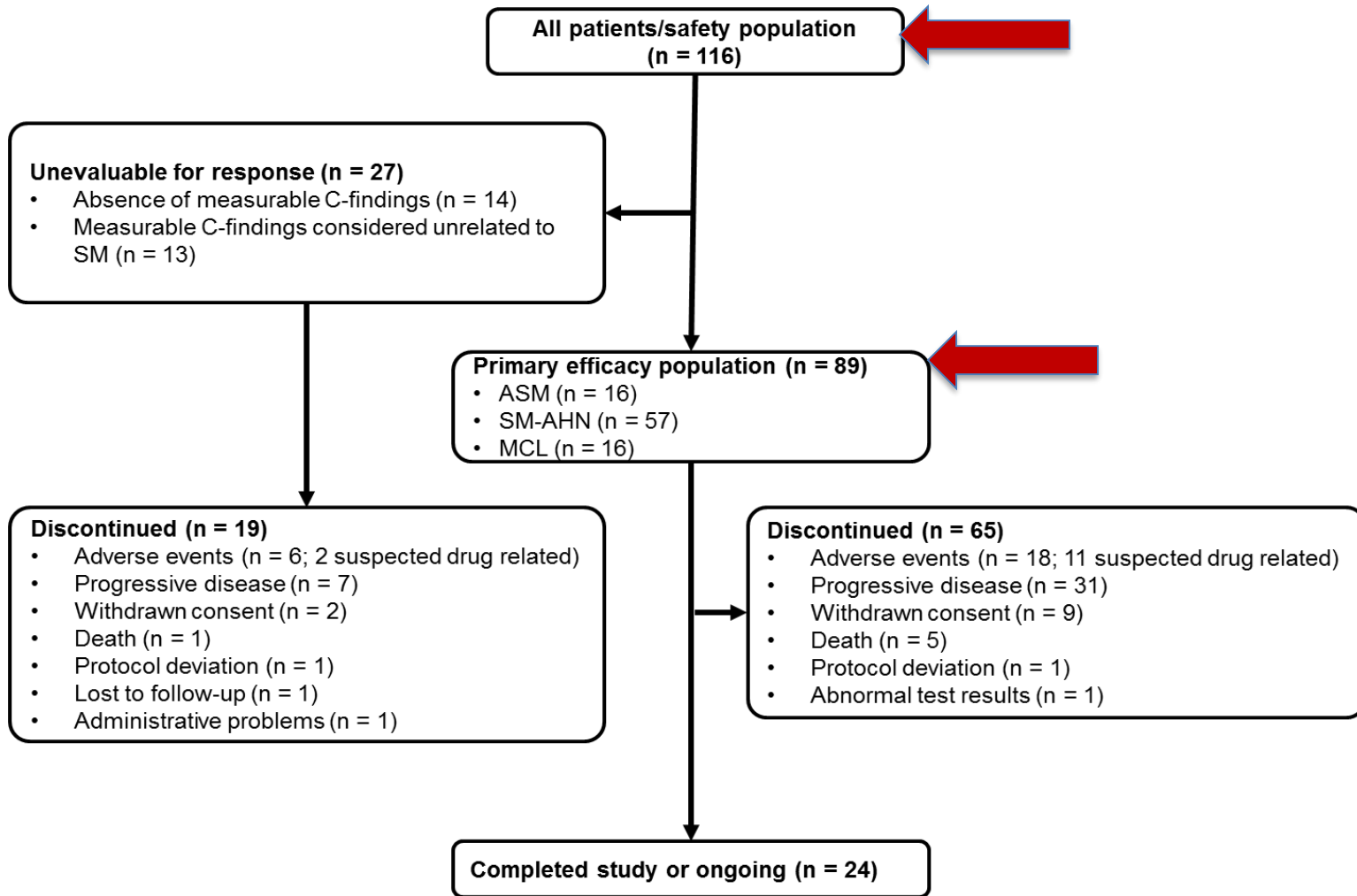
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Efficacy and Safety of Midostaurin in Advanced Systemic Mastocytosis

Jason Gotlib, M.D., Hanneke C. Kluin-Nelemans, M.D., Ph.D.,  
Tracy I. George, M.D., Cem Akin, M.D., Ph.D., Karl Sotlar, M.D.,  
Olivier Hermine, M.D., Ph.D., Farrukh T. Awan, M.D., Elizabeth Hexner, M.D.,  
Michael J. Mauro, M.D., David W. Sternberg, M.D., Ph.D.,  
Matthieu Villeneuve, M.Sc., Alice Huntsman Labeled, Ph.D.,  
Eric J. Stanek, Pharm.D., Karin Hartmann, M.D., Hans-Peter Horny, M.D.,  
Peter Valent, M.D., and Andreas Reiter, M.D.

ABSTRACT



# Baseline Patient and Disease Characteristics

**Table 1. Baseline Patient and Disease Characteristics.\***

Characteristic	Intention-to-Treat Population (N = 116)	Primary Efficacy Population (N = 89)
Age — yr		
Median	63	64
Range	25–82	25–82
Male sex — no. (%)	76 (66)	57 (64)
ECOG performance status — no. (%)†		
0 or 1	77 (66)	57 (64)
2 or 3	39 (34)	32 (36)
No. of previous therapies — no. of patients (%)		
0	64 (55)	52 (58)
1	29 (25)	21 (24)
2	15 (13)	12 (13)
≥3‡	8 (7)	4 (4)
Subtype of advanced systemic mastocytosis — no. (%)		
Aggressive systemic mastocytosis	ND	16 (18)
Systemic mastocytosis with an AHN	ND	57 (64)
Mast-cell leukemia	21 (18)	16 (18)
<i>KIT</i> D816 mutation status — no. (%)		
Positive	98 (84)	77 (87)§
Negative	13 (11)	10 (11)
Unknown	5 (4)	2 (2)
Bone marrow mast-cell burden — %		
Median	40	50
Range	3–98	8–98
Serum tryptase level — µg/liter		
Median	200	236
Range	2–12,069	27–12,069
No. of C-findings per patient — no. of patients (%)¶		
1	31 (27)	31 (35)
2	20 (17)	20 (22)
≥3	38 (33)	38 (43)

\* Data on additional baseline characteristics are provided in Table S6 in the Supplementary Appendix. AHN denotes associated hematologic neoplasm, and ND not determined.

† Values for the Eastern Cooperative Oncology Group (ECOG) performance status range from 0 to 5, with 0 indicating no symptoms and higher numbers indicating increasing tumor-associated disability.

‡ In some patients with SM-AHN, therapy was directed toward the associated hematologic neoplasm.

§ A total of 73 patients were positive for the *KIT* D816V mutation, 3 were positive for the *KIT* D816Y mutation, and 1 was positive for the *KIT* D816L mutation.

¶ Clinical findings that are related to organ damage from infiltrating mast cells are referred to as C-findings.<sup>4,5</sup> Only measurable C-findings were eligible for this study: transfusion-independent and transfusion-dependent anemia and thrombocytopenia, neutropenia, liver-function abnormalities (increased levels of alanine aminotransferase, aspartate aminotransferase, or total bilirubin), hypoalbuminemia, and medically documented loss of at least 10% of body weight within 6 months before study entry.

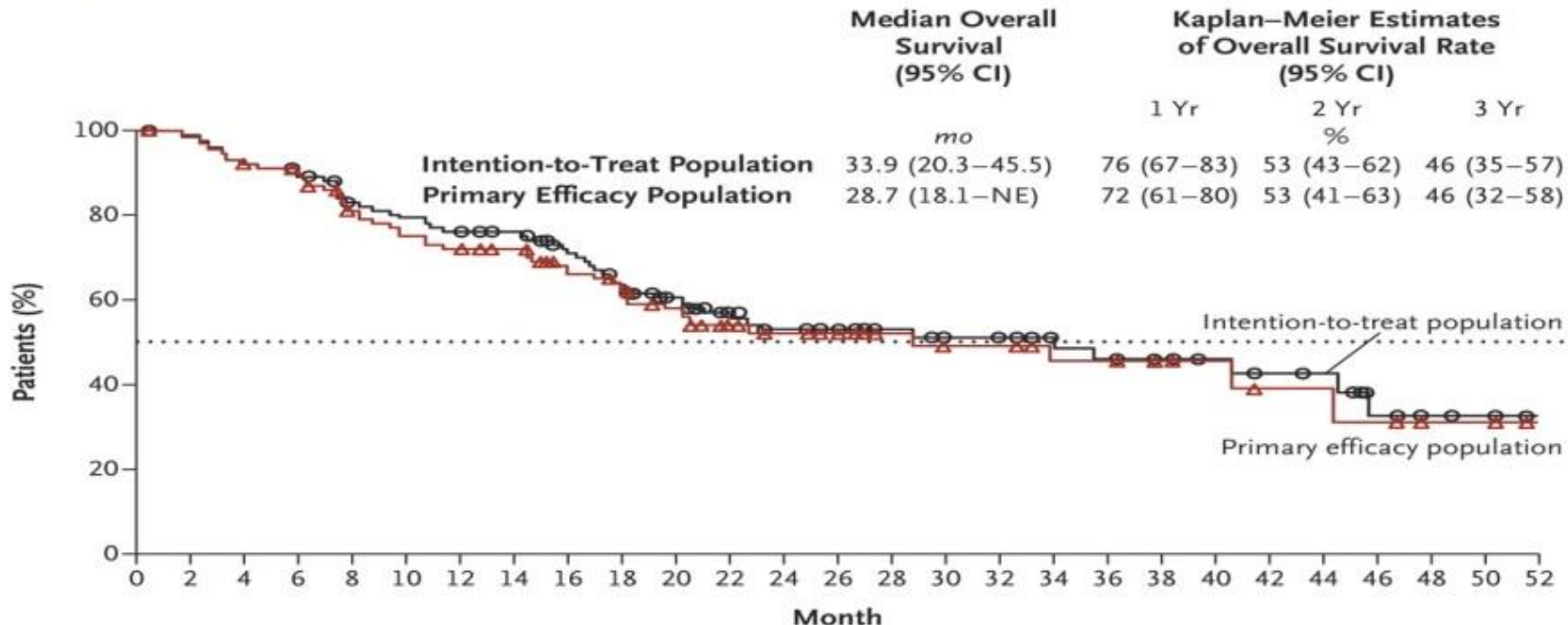
**Table 2. Best Overall Response to Midostaurin in the Primary Efficacy Population.\***

Variable	Any Subtype of Advanced Systemic Mastocytosis (N = 89)	Aggressive Systemic Mastocytosis (N = 16)	Systemic Mastocytosis with an AHN (N = 57)	Mast-Cell Leukemia (N = 16)
Major or partial response as best overall response				
Patients with response — no.	53	12	33	8
Overall response rate (95% CI) — %	60 (49–70)	75 (48–93)	58 (44–71)	50 (25–75)
Duration of response — mo				
Median	24.1	NR	12.7	NR
95% CI	10.8–NE	24.1–NE	7.4–31.4	3.6–NE
Best overall response — no. (%)				
Major response	40 (45)	10 (62)	23 (40)	7 (44)
Complete remission	0	0	0	0
Incomplete remission	19 (21)	6 (38)	9 (16)	4 (25)
Pure clinical response	15 (17)	4 (25)	9 (16)	2 (12)
Unspecified	6 (7)	0	5 (9)	1 (6)
Partial response	13 (15)	2 (12)	10 (18)	1 (6)
Good partial response	11 (12)	1 (6)	10 (18)	0
Minor partial response	2 (2)	1 (6)	0	1 (6)
Stable disease	11 (12)	1 (6)	7 (12)	3 (19)
Progressive disease	10 (11)	1 (6)	6 (11)	3 (19)
Patient could not be evaluated for response†	15 (17)	2 (12)	11 (19)	2 (12)



# Overall Survival

A Overall Survival



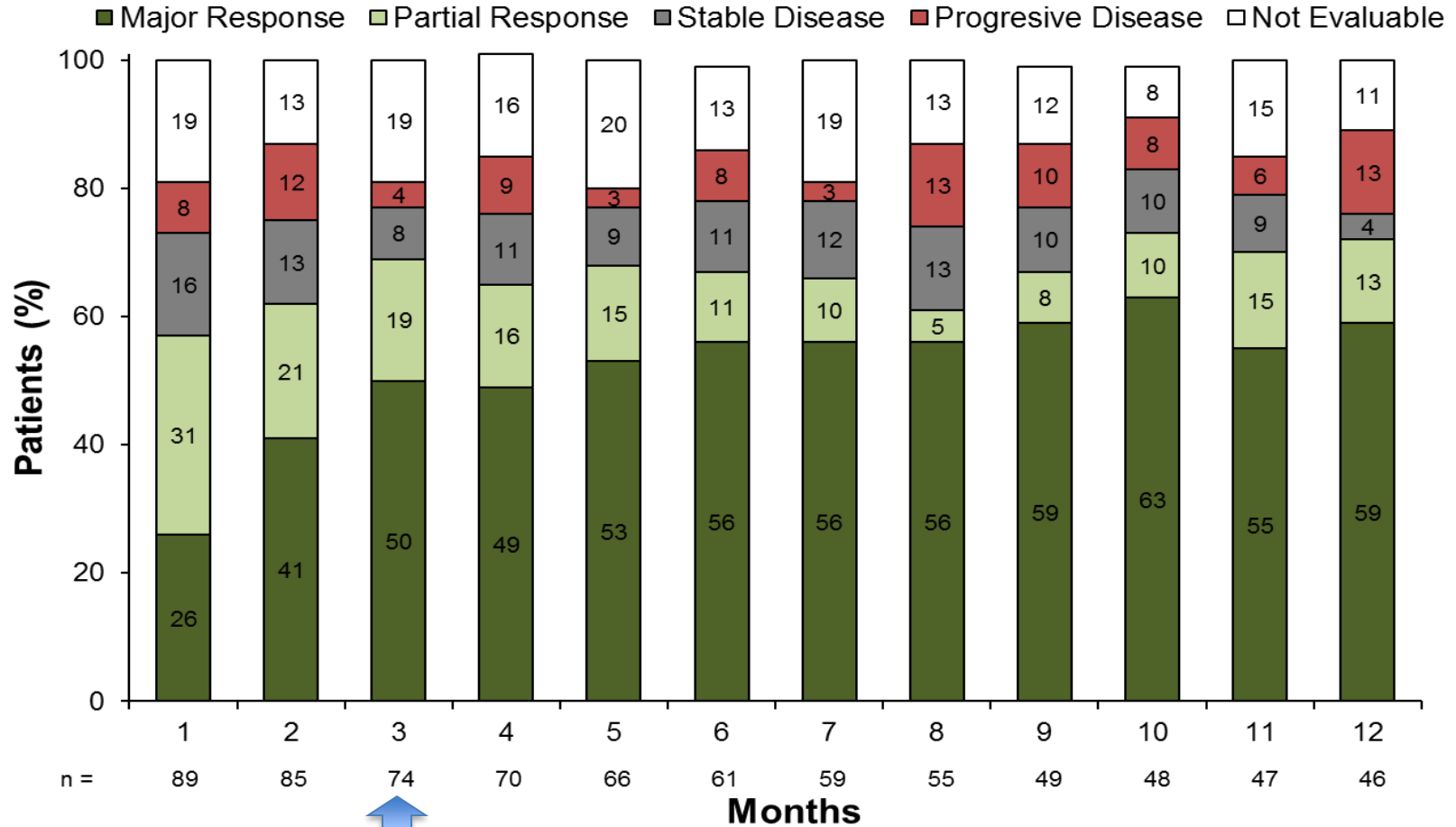
**No. at Risk**

Intention-to-treat population	116	113	105	102	91	87	83	80	70	61	54	44	38	36	28	25	24	20	19	15	13	11	10	5	3	2	0
Primary efficacy population	89	87	80	77	66	62	59	56	48	43	38	30	26	24	17	15	15	12	12	8	7	5	5	4	2	2	0

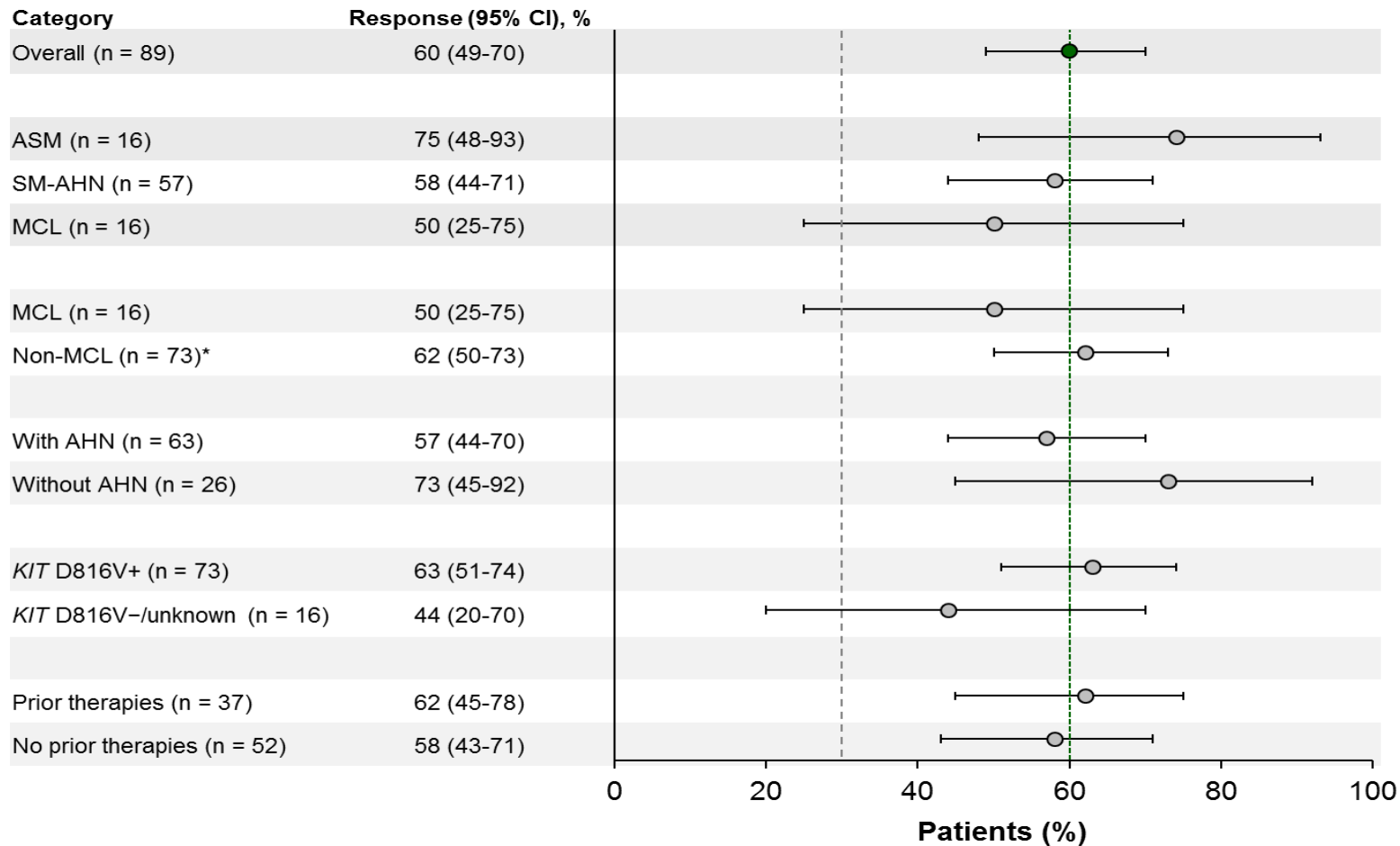




# Response over Time

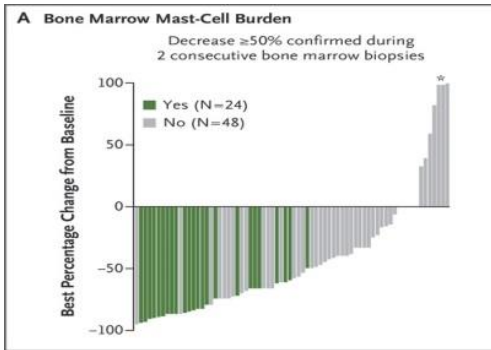


# Overall Response Rate by Subgroups

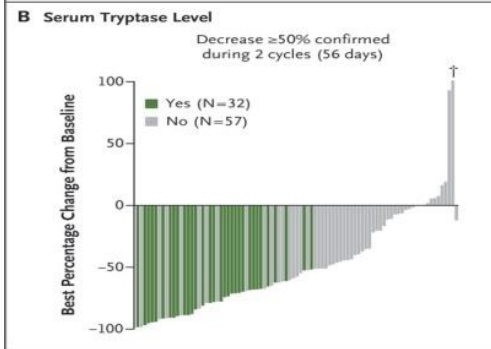




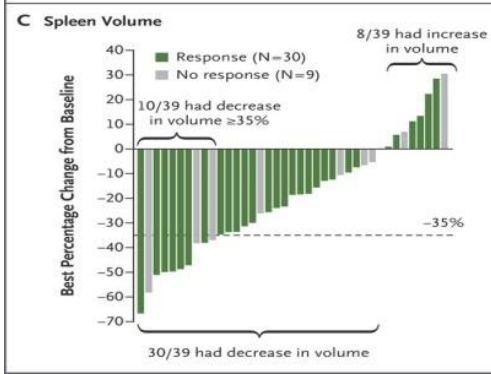
# Clinicopathological Measures of Response



**Bone marrow  
mast cell burden**

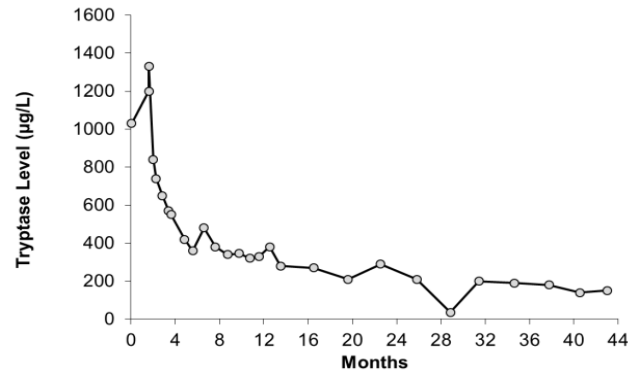
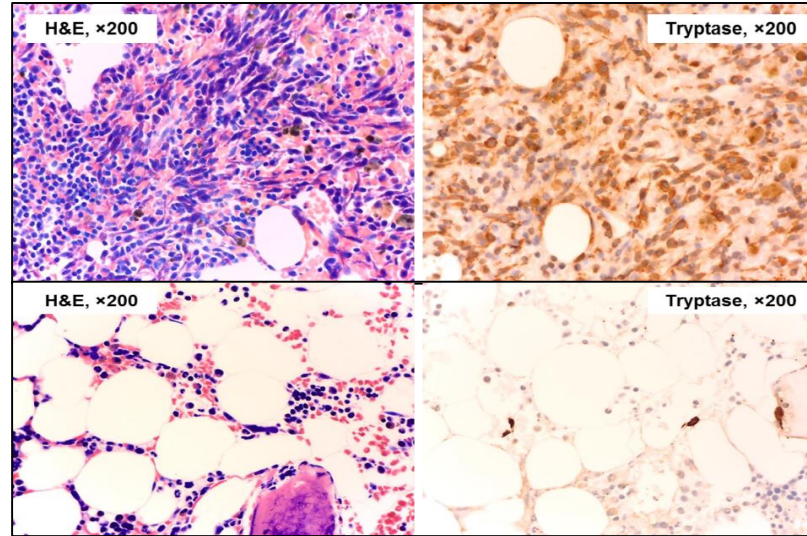


**Serum tryptase**



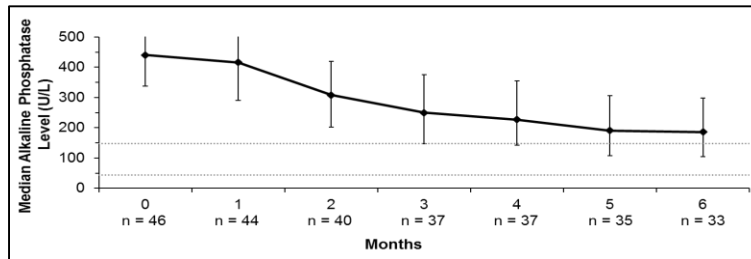
**Spleen volume**

# Histologic Regression in ASM patient

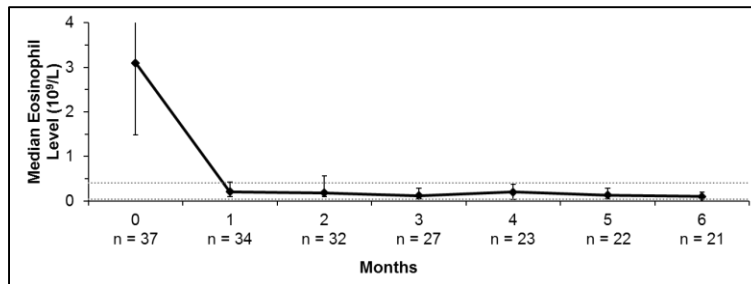


# Improvements in Alkaline Phosphatase, Eosinophil, and Monocyte Levels

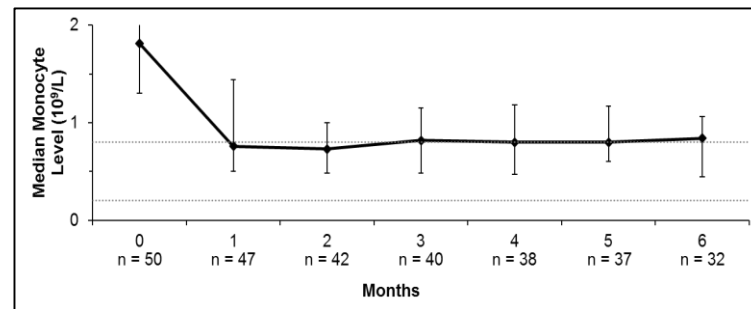
**Alk Phos**



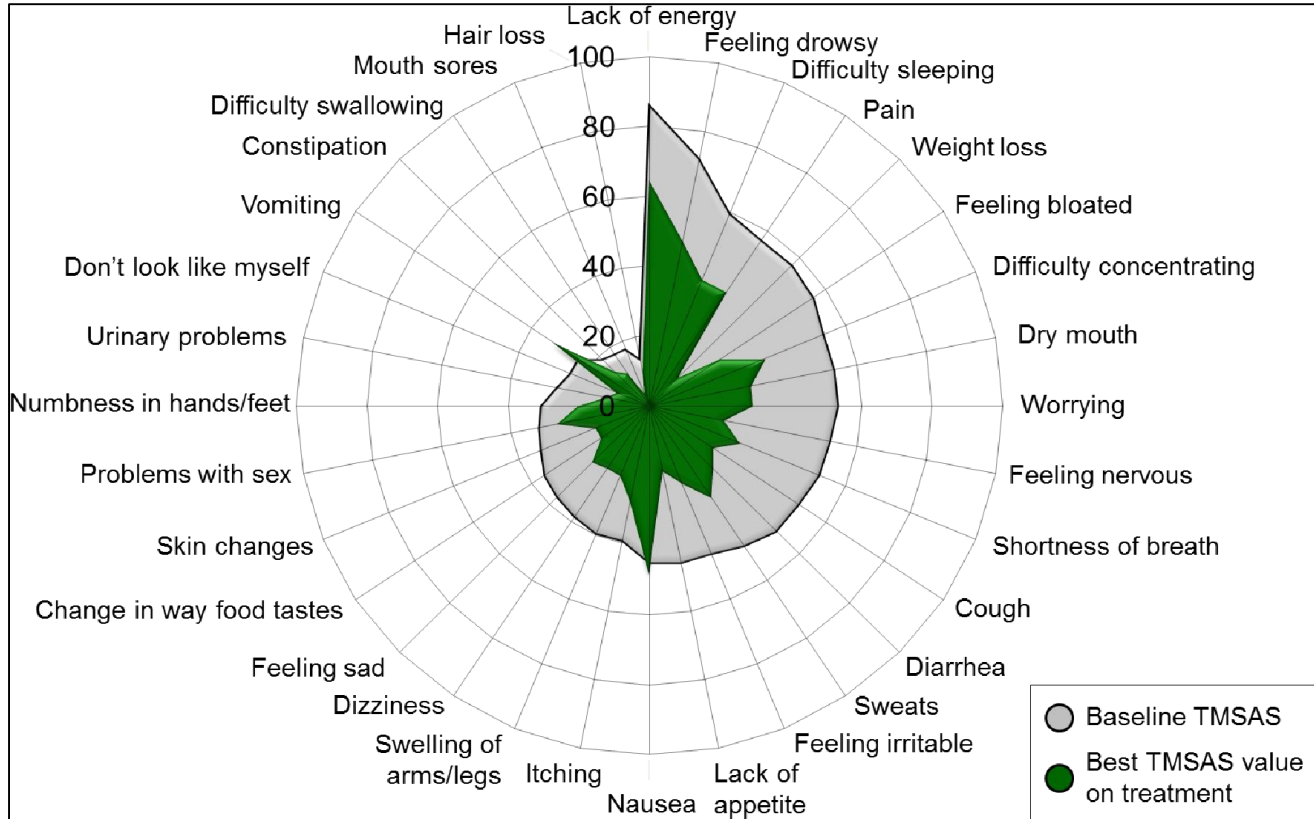
**Eos**



**Monos**



# Improvements in Quality of Life

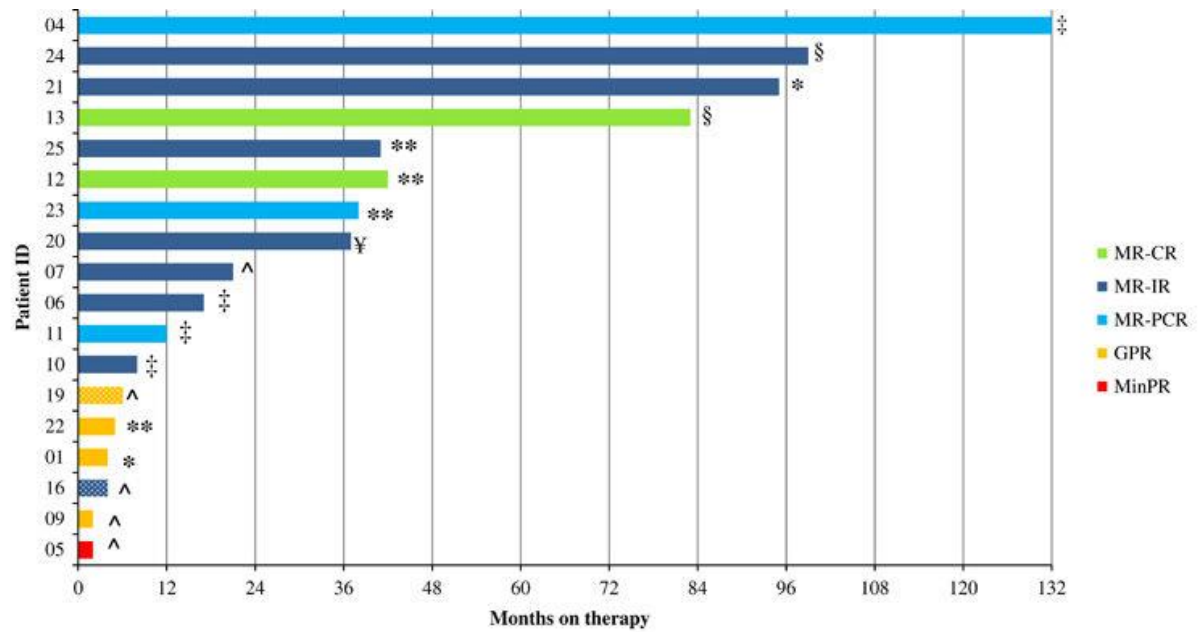


# Study Conclusions

- *Midostaurin can:*
  - Reverse organ damage
  - Decrease splenomegaly
  - Decrease BM mast cells
  - Improve patient-reported symptoms and quality of life



# Midostaurin in advanced SM, 10 year follow-up



## Study status/reason for discontinuation (# of patients)<sup>†</sup>

- § Continuing treatment (n=2)
- \* Adverse event: Grade 3 or 4 thrombocytopenia (n=2)
- \*\* Serious adverse event: sepsis (n=3), inflammatory mixed neuropathy/myopathy and altered mental status (n=1)
- ¥ Withdrew consent (n=1)
- ^ Unsatisfactory therapeutic effect; discontinued per investigator discretion (n=5)
- ‡ Disease progression (n=4)

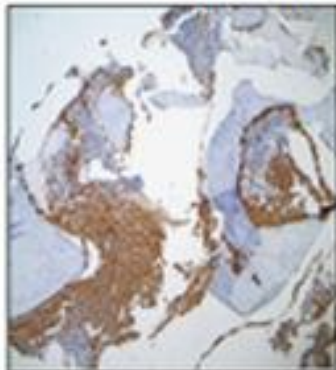
Median duration of treatment (months)	
median	19
range	2-132

<sup>†</sup> Data through 3/1/2017; best response at any time on therapy

Solid bars are *KIT* D816 mutation-positive, two patterned bars are *KIT* D816 mutation-negative

**ID# 24**

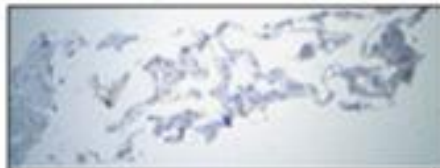
**Baseline, CD117: 70%**



**End Cycle 3, CD117: 50%**



**End Cycle 6, CD117: 10%**



**ID# 07**

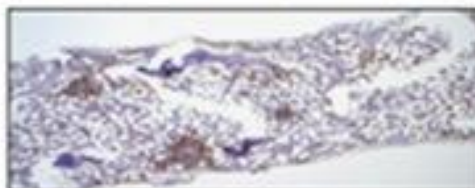
**Baseline, MC tryptase: 50%**



**End Cycle 2, MC tryptase: 30%**

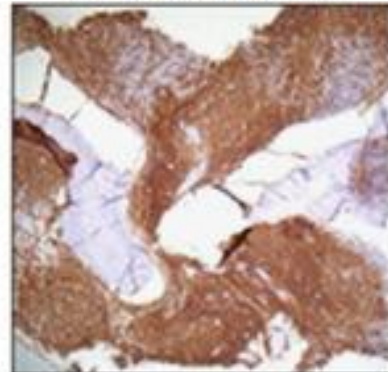


**End Cycle 18, MC tryptase: 10-20%**

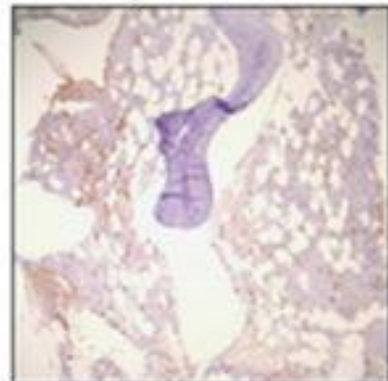


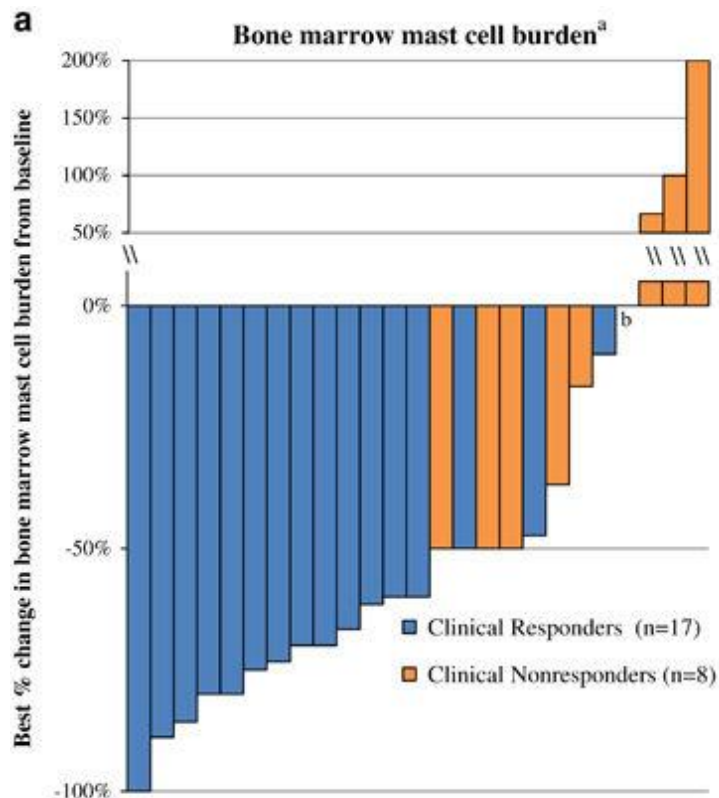
**ID# 12**

**Baseline, CD117: 70%**



**End Cycle 3, CD117: 5%**

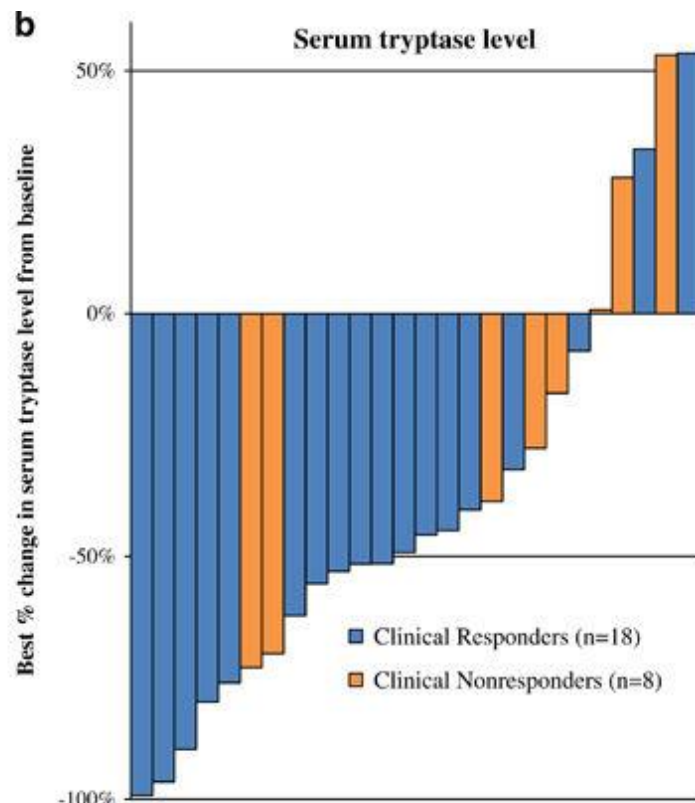




**Best % change in bone marrow mast cell burden:  
Median -60% (range -100 to 200%)**

<sup>a</sup> N=25 instead of 26. One responder did not have quantification of bone marrow mast cells at baseline; described as 'focally involved'.

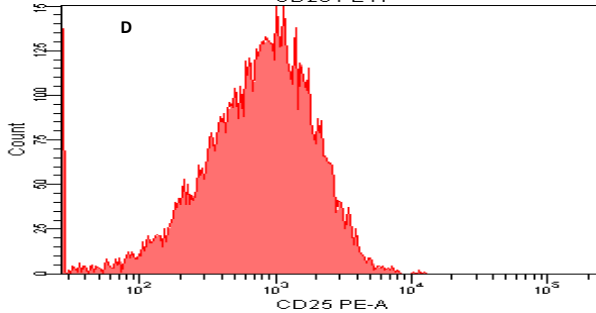
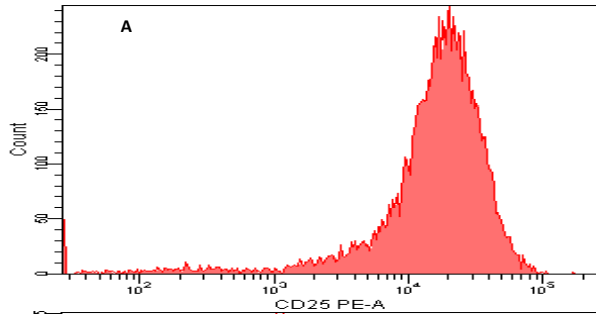
<sup>b</sup> Responder with best value of 0% change in bone marrow mast cells vs baseline



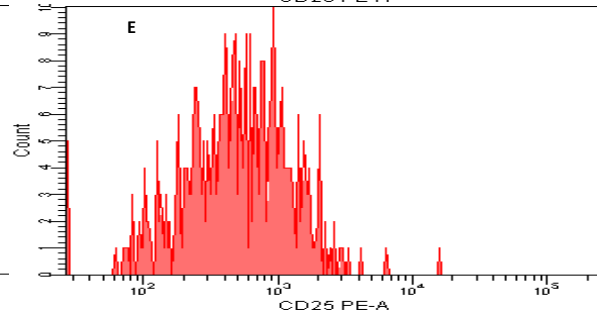
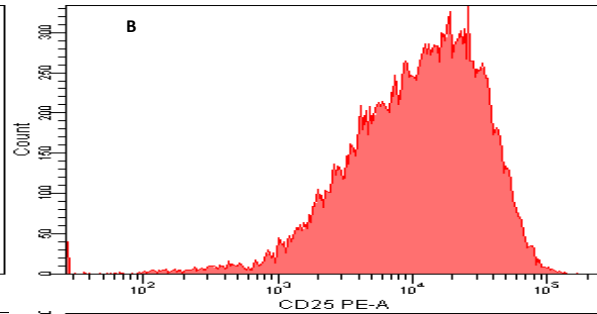
**Best % change in serum tryptase level:  
Median -47% (range -99 to 54%)**

# Midostaurin treatment is associated with a significant decrease in CD25 expression on neoplastic mast cells

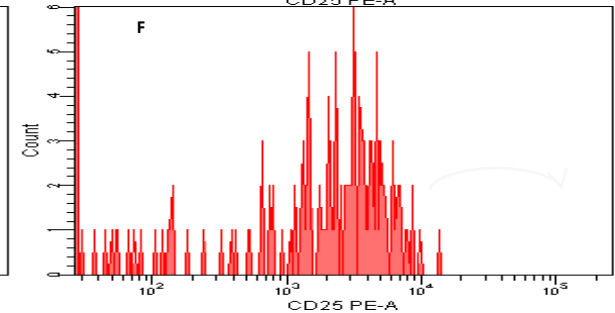
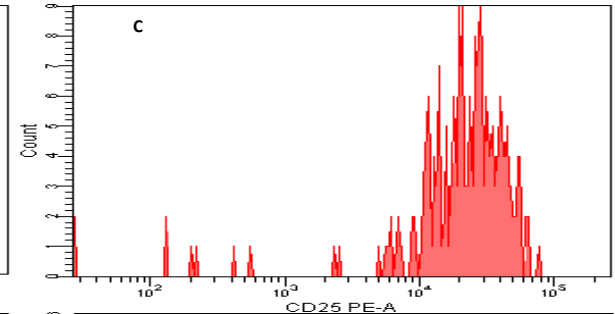
## Patient #1



## Patient #2

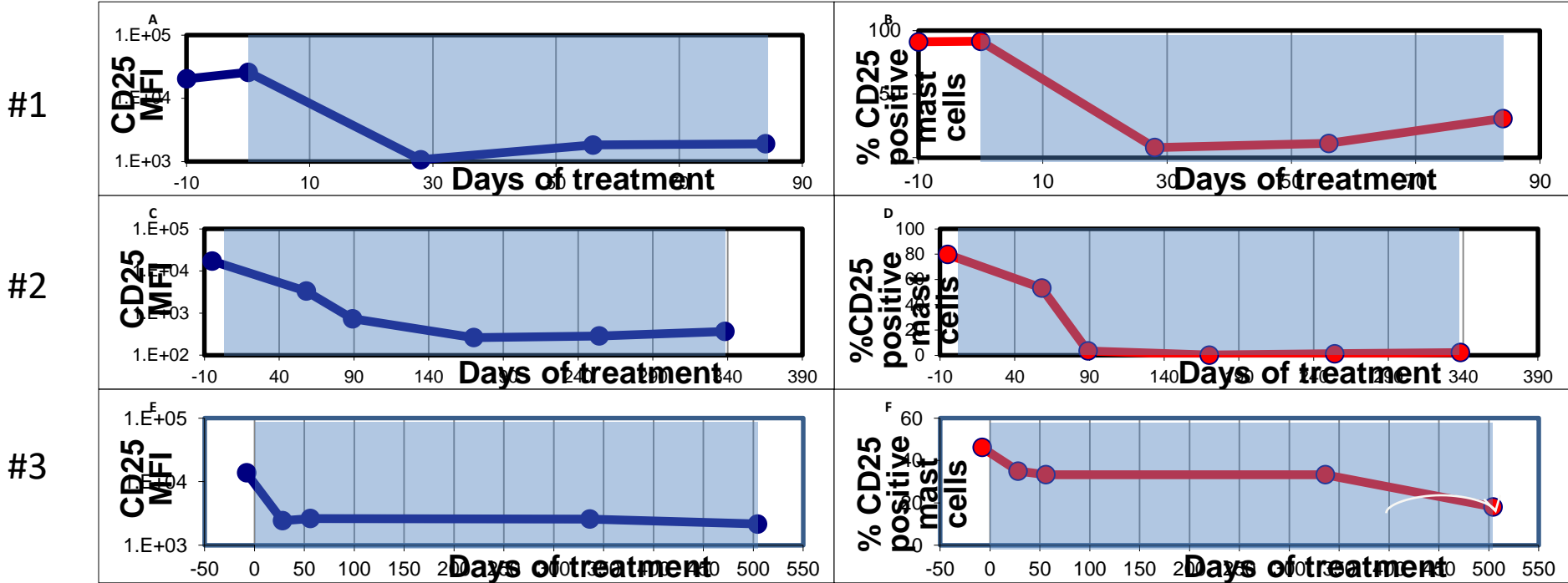


## Patient #3



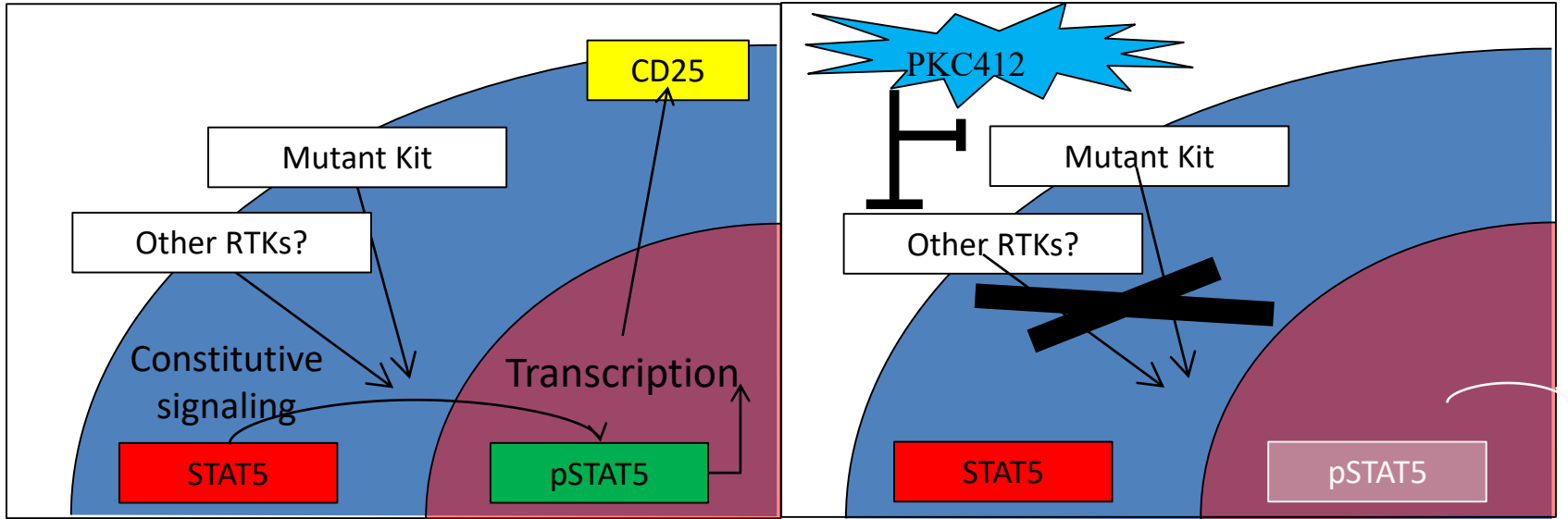
CD25 expression on neoplastic mast cells by flow cytometry in patients #1, #2, and #3 before (A-C) and on day 28 (patient #1, D), day 89 (patient #2, E), and day 336 (patient #3, F) of midostaurin therapy.

# Midostaurin therapy is associated with sustained decreases in CD25 expression



CD25 expression on neoplastic mast cells by mean fluorescence intensity (MFI; A, C, E) and percent of mast cells positive for CD25 (B, D, F) over time in patient #1 (A-B), patient #2 (C-D), and patient #3 (E-F). The shaded area indicates time on midostaurin therapy.

# Proposed mechanism for midostaurin-induced CD25 downregulation

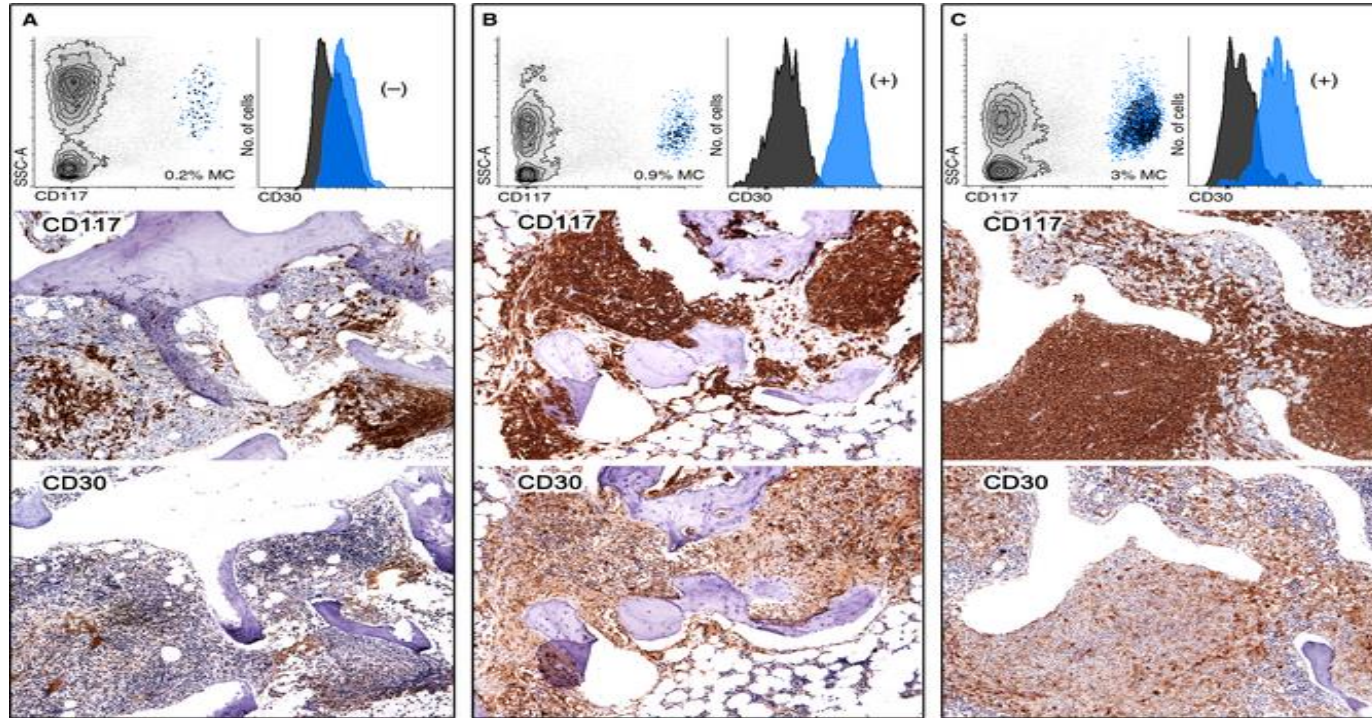


Changes in the intracellular localization of STAT5 with midostaurin

# Outline

- Updates on classification
- Advanced mastocytosis
- A case report
- Clinical trials
- **Other potential therapies**

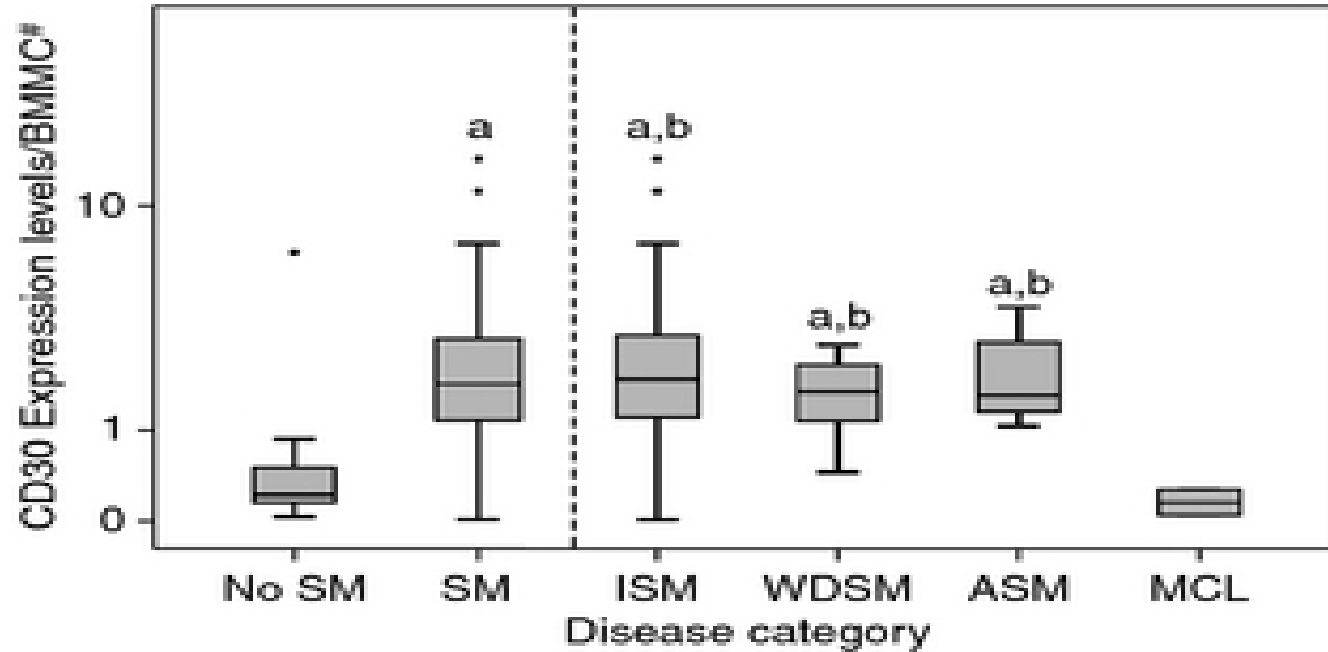
# CD30 expression in systemic mastocytosis



JM Morgado, O Perbellini, RC Johnson, C Teodosio, A Matito, I Alvarez-Twose, P Bonadonna, A Zamo M Jara-Acevedo, A Mayado, A Garcia-Montero, M Mollejo, TI George, R Zanotti, A Orfao, L Escribano, L Sanchez-Munoz. CD30 expression by bone marrow mast cells from different diagnostic variants of systemic mastocytosis. *Histopathology* 2013;63(6):780-7.

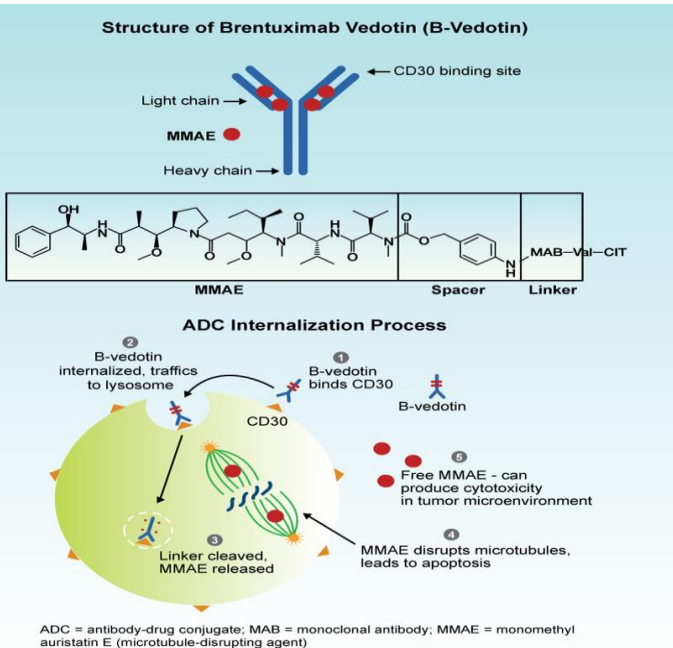


# CD30 expression in systemic mastocytosis



JM Morgado, O Perbellini, RC Johnson, C Teodosio, A Matito, I Alvarez-Twose, P Bonadonna, A Zamo M Jara-Acevedo, A Mayado, A Garcia-Montero, M Mollejo, TI George, R Zanotti, A Orfao, L Escribano, L Sanchez-Munoz. CD30 expression by bone marrow mast cells from different diagnostic variants of systemic mastocytosis. *Histopathology* 2013;63(6):780-7.

# Clinical trial with anti-CD30 drug does *not* demonstrative clinical activity in advanced systemic mastocytosis



10 patients:

-8 stable disease

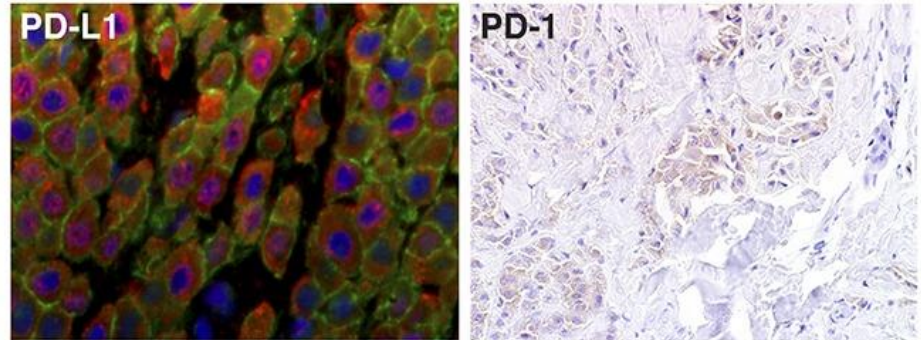
-1 progressive disease

-1 not evaluable due to early death unrelated to study

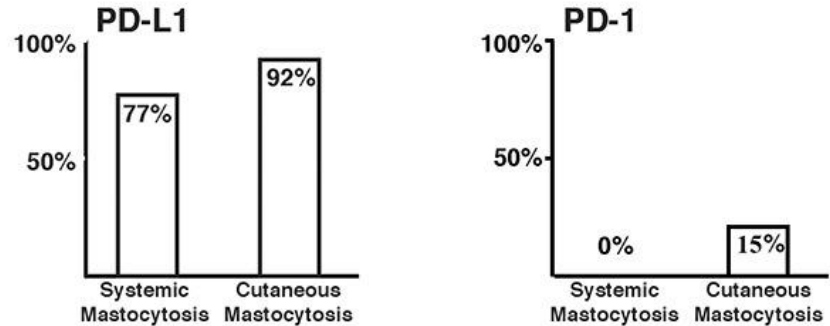
Baird JH, Verstovsek S, George TI, Reyes I, Abuel J, Perkins C, Langford C, Schroeder K, Gotlib J. Phase 2 study of Brentuximab Vedotin in patients with advanced systemic mastocytosis. ASH 2017.



## PD-L1 and PD-1 Expression in Mastocytosis Subtypes



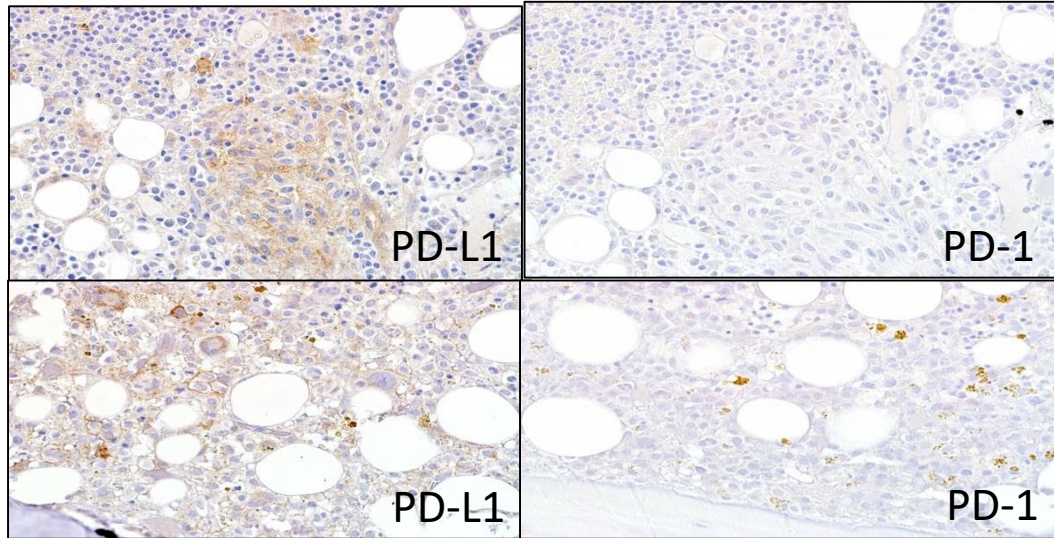
Percentage of Patient Cases Positive for:



Hatch EW, Geeze MB, Martin C, Salama ME, Hartmann K, Eisenwort G, Blatt K, Valent P, Gotlib J, Lee JH, Chen L, Ward HH, Lidke DS, George TI (2018). Variability of PD-L1 expression in mastocytosis. *Blood Adv* 2(3), 189-199.

# Immunohistochemistry

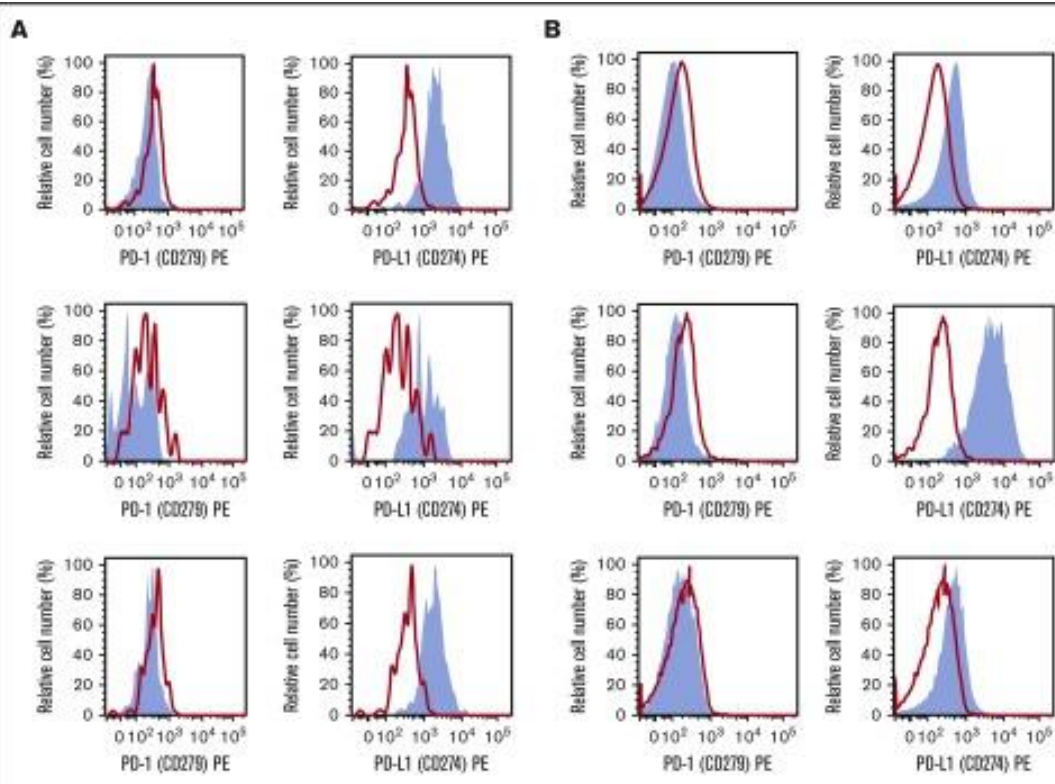
Smoldering systemic mastocytosis



Mast cell leukemia

# Flow cytometry

Indolent SM



Indolent SM

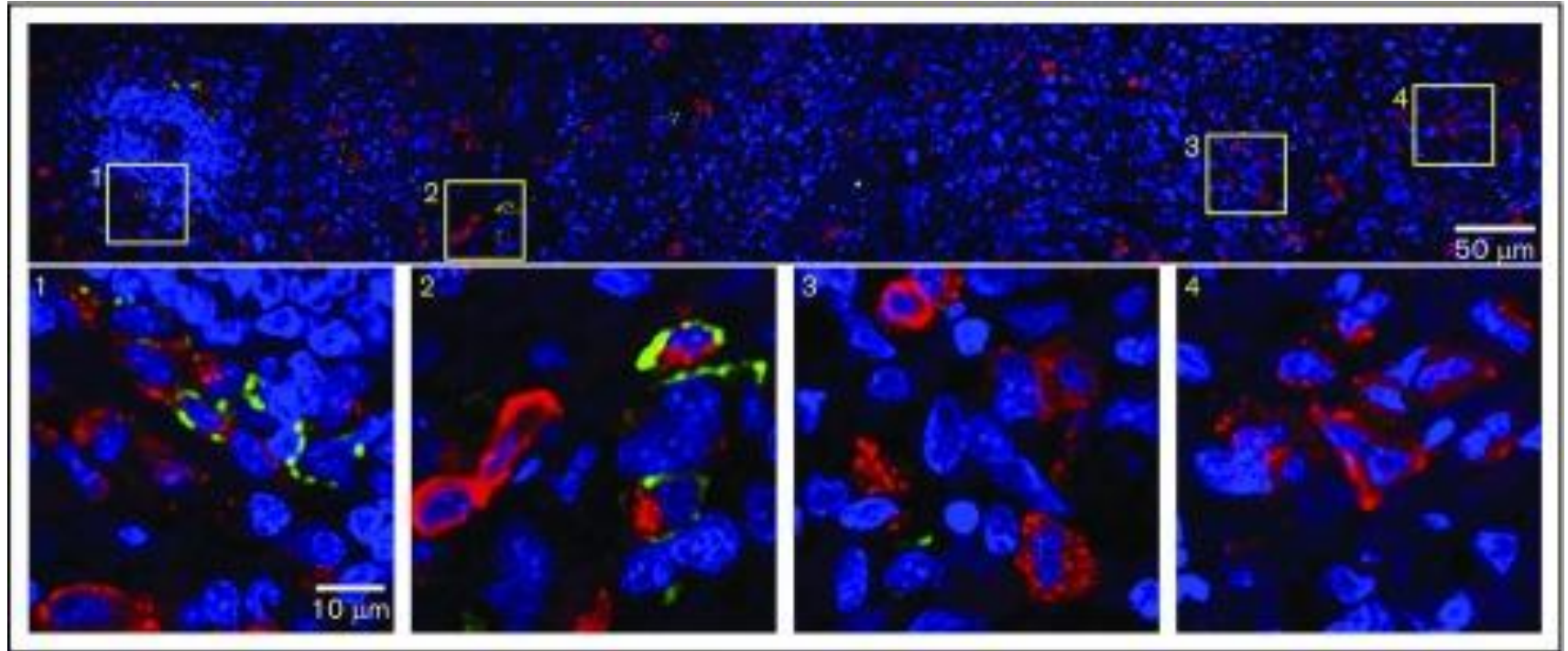
Mast cell leukemia

Mast cell leukemia

Indolent SM

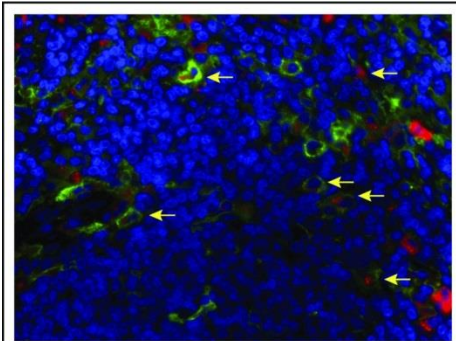
Aggressive SM

# Multiplex immunohistofluorescence

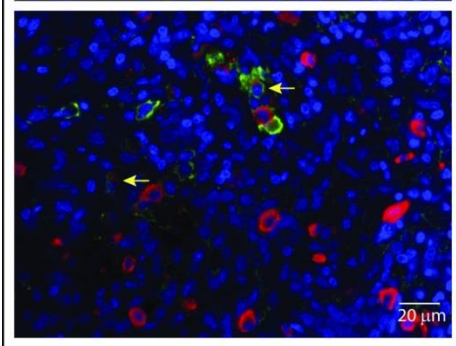
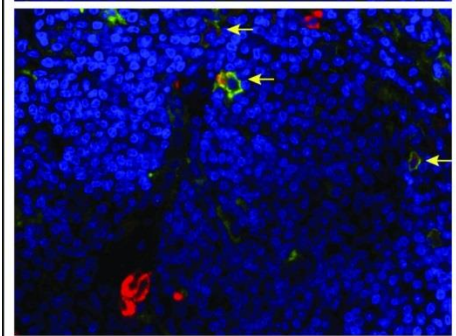


Mast cell leukemia, spleen

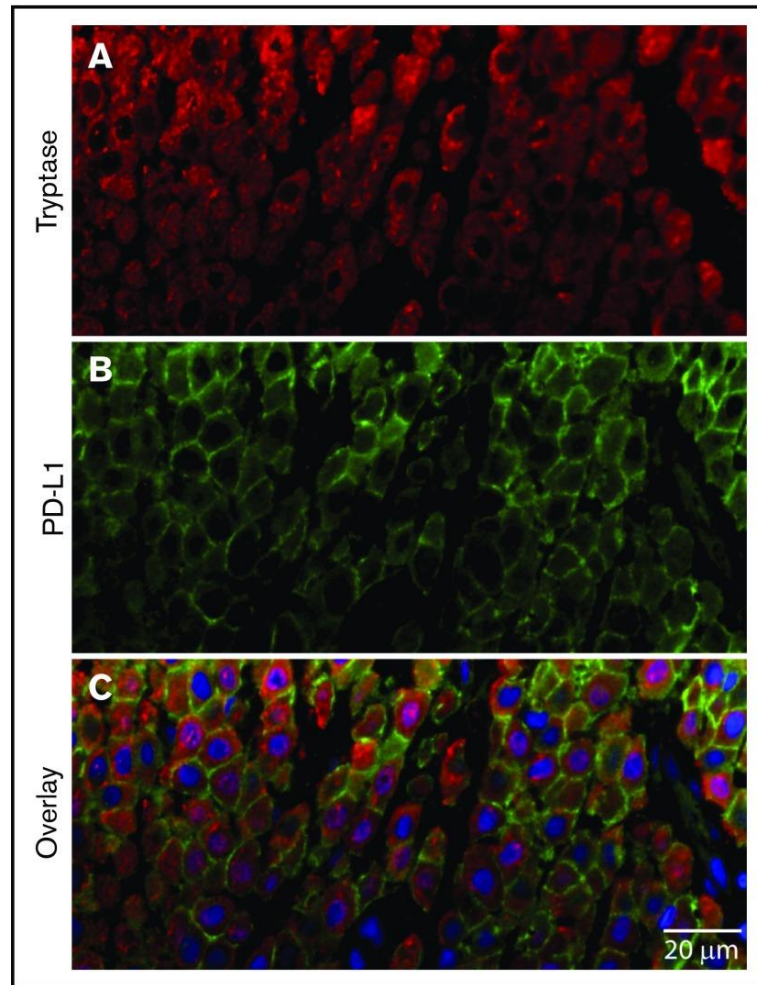
Tryptase (red), PDL1 (green)



Tryptase (red)  
PDL1 (green)



Mast cell  
leukemia,  
spleen



Cutaneous mastocytosis

# PD-1/PD-L1 are novel therapeutic targets for mastocytosis

Diagnosis	PD-L1 expression	PD-1 expression
SM	17/22 (77%)	0/25
CM	23/25 (92%)	4/27 (15%)
MML	1/2	0/2
MMAS	0/3	0/3
MPN	0/16	0/17
MDS	0/18	0/18
MDS/MPN	0/5	0/5
Healthy/ reactive BM	0/15	0/21



# PD-1/PD-L1 are novel therapeutic targets for mastocytosis



Diagnosis	PD-L1 expression	PD-1 expression
SM	17/22 (77%)	0/25
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MPN	0/16	0/17
MDS	0/18	0/18
MDS/MPN	0/5	0/5
Healthy/ reactive BM	0/15	0/21

<b>MCL</b>	<b>3/3 (100%)</b>
<b>ASM</b>	<b>2/2 (100%)</b>
<b>SM-AHN</b>	<b>9/12 (75%)</b>
<b>SSM</b>	<b>1/2 (50%)</b>
<b>ISM</b>	<b>3/4 (75%)</b>

# Conclusions

- Updates on classification
- Advanced mastocytosis
- A case report
- Clinical trials
- Other potential therapies

# *Thank you collaborators!*

Jason Gotlib  
Dan Arber  
Susan Atwater  
Bruno Medeiros  
Athena Cherry



Natasha Savage  
Farrukh Awan



REMA (Spanish  
Network on  
Mastocytosis)



Chris Corless  
Ilana Kepten  
Jeffrey Tyner



Peter Valent

Timothy Graubert



Dan Deangelo



Eric Hsi



Hans-Peter Horny  
Karl Sotlar