

MASTOCITOSI E BPDCN: LE DIAGNOSI DIFFICILI

BOLOGNA, ROYAL HOTEL CARLTON | 12 OTTOBRE 2026



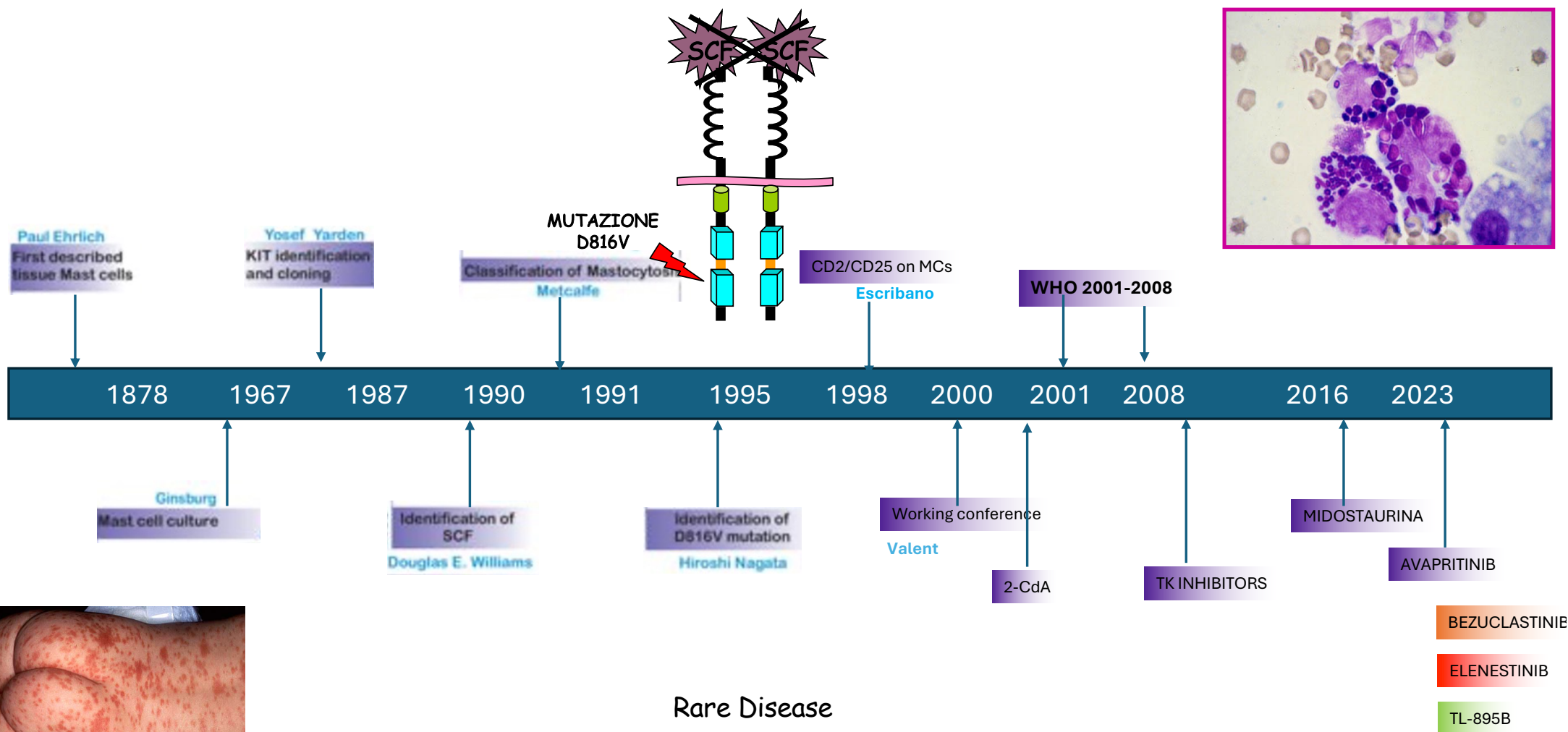
RESPONSABILI SCIENTIFICI:
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Mastocitosi:

Panoramica oggi

Dr. Ssa Michela Rondoni

AUSL ROMAGNA U.O. C. Ematologia Ravenna



Rare Disease

Prevalence in Europe: 0,9-1,3:10.000 adulti

Inserita in Elenco malattie rare in Italia dal 2015 (RD0081)

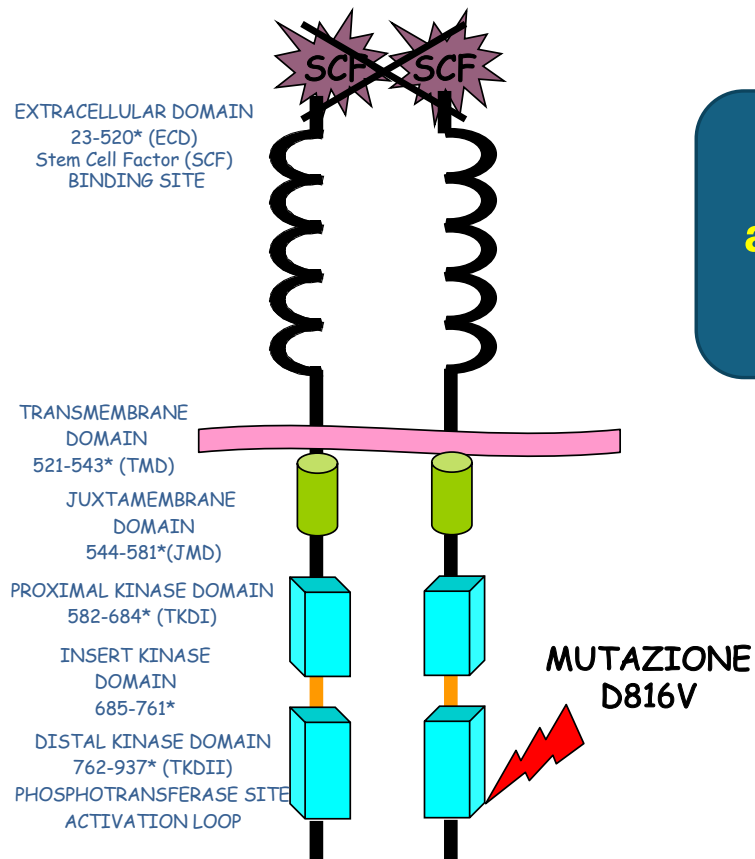
BEZUCLASTINIB

ELENESTINIB

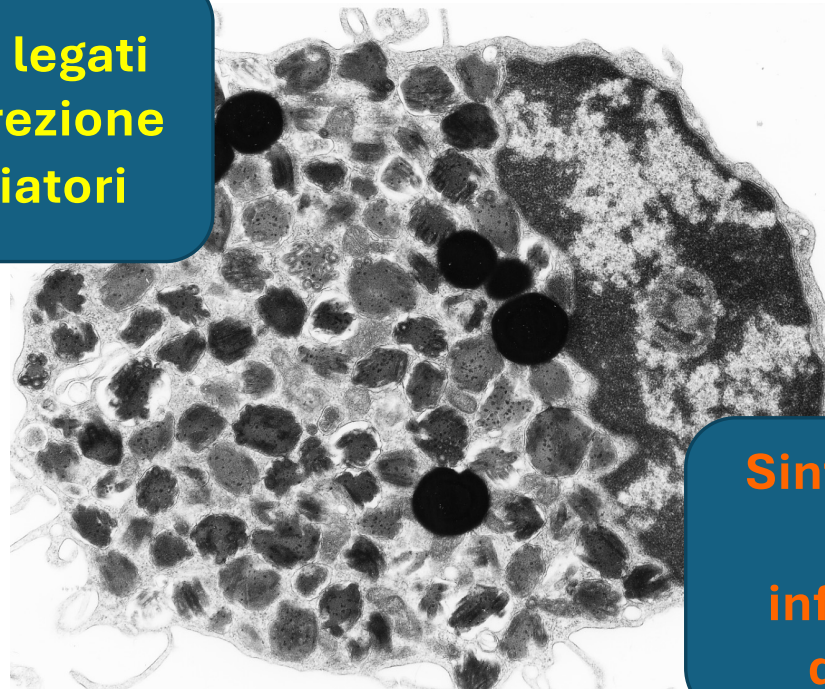
TL-895B

Dal Mastocita alle Mastocitosi

La mutazione del gene c-kit provoca l'attivazione costitutiva del recettore KIT, rendendolo indipendente dal fattore di crescita SCF determinando la proliferazione clonale incontrollata dei mastociti in organi specifici come cute, ossa, midollo osseo e tratto gastrointestinale

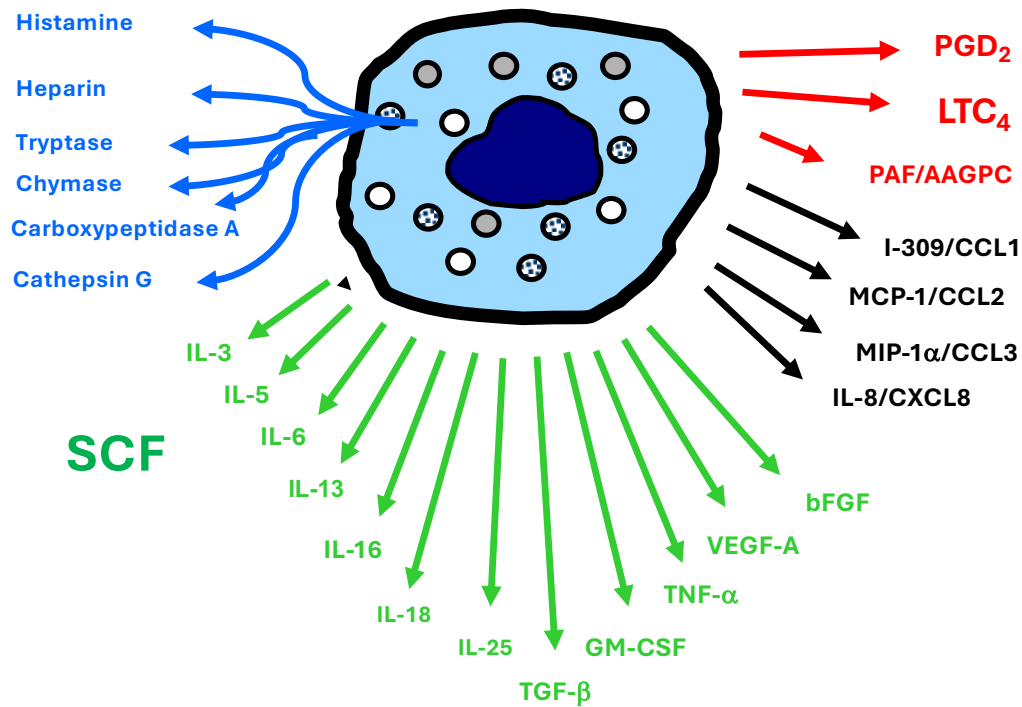


**Sintomi legati
alla secrezione
di mediatori**



**Sintomi legati
alla
infiltrazione
d'organo**

Degranulazione mastocitaria e Sintomi



Stimuli that elicit mast cell degranulation:
product of complement activation, neuropeptides, bacterial products,
cytokines, animal venom components, chemical agents, physical stimuli,
morphine and other narcotics

Mediatori	Meccanismo d'azione proposto	Reperti clinici e patologici considerati correlati al mediatore
Istamina	- Recettori H₁ - Recettori H₂	- Ipotensione, cefalea, edema, rossore, orticaria, broncocostrizione - Gastrite, ulcera peptica, diarrea, dolore addominale, crampi
Triptasi	Attività enzimatica	Osteoporosi, alterazioni della coagulazione
Eparina	Attività anticoagulante e cofattore per altri mediatori mastocitari	Alterazioni della coagulazione, osteoporosi
Leucotrieni	Recettori CysLT₁/CysLT₂	Rossore, orticaria, ipotensione, broncospasmo, diarrea
TNF-α, IL-6, altri		Dolori ossei e muscolari, stanchezza, affaticamento

Sintomi legati alla secrezione di mediatori

- Flushing
- Orticaria
- Episodi di ipotensione/Anafilassi - da IMENOTTERI



- da farmaci (β -lattamici, FANS ed anestetici)

- da alimenti (alcol, conservanti)

- Osteoporosi severa
- Nausea, vomito e diarrea
- Crampi addominali
- Cefalea



Triptasi elevata

Sintomi legati alla infiltrazione d'organo

Espansione midollare	→	Alterazioni dell'emocromo (citopenia, monocitosi, eosinofilia, SM-AHN)
Epatosplenomegalia	→	Alterazioni indici funzionalità epatica Ascite
Interessamento G.I.	→	Malassorbimento
Osteolisi (> 2 cm)	→	Fratture

*B and C-
findings*

Mastocitosi Sistemica: diagnosi

Criterio maggiore:

Infiltrati mastocitari multifocali densi (>15 mastociti aggregati) in sezioni istologiche di midollo osseo e/o di altri organi extracutanei

Criteri minori:

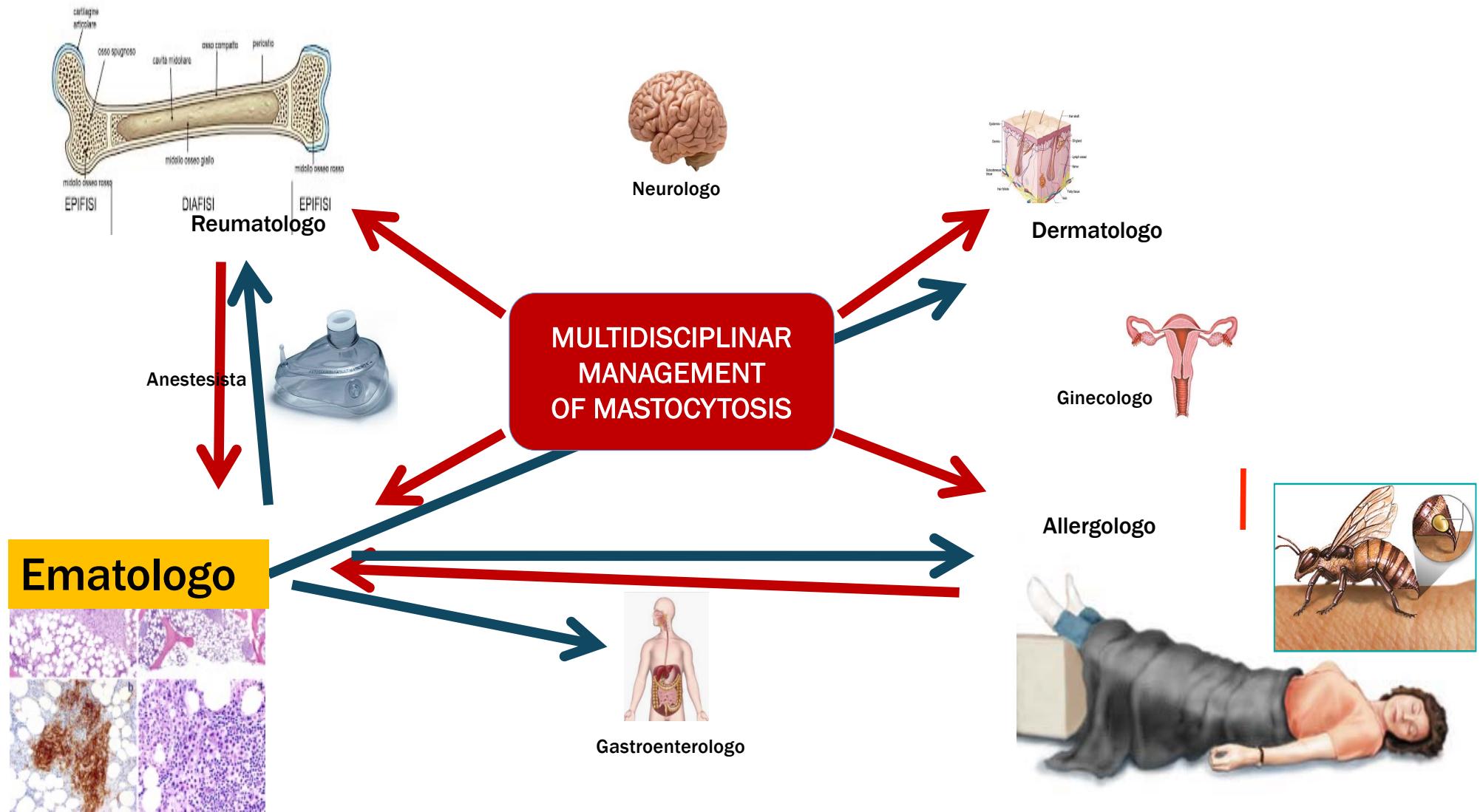
1. Presenza di > 25% di mastociti di forma fusata in infiltrati mastocitari rilevati in sezioni istologiche di midollo osseo o altri organi extracutanei, oppure > 25% di mastociti immaturi o atipici negli strisci di midollo osseo
2. Positività della mutazione puntiforme del codone 816 del KIT (Asp816→Val) o in altre regioni note di KIT nel midollo osseo o in altri organi extracutanei
3. Positività per CD2 e/o CD25, e/o CD30, oltre che per gli altri markers mastocitari, in mastociti del midollo osseo, del sangue o di altri organi extracutanei
4. Concentrazioni sieriche di triptasi persistentemente > 20 ng/ml (purchè non ci sia un altro disordine mieloidale associato, in questo caso questo parametro non può essere considerato). In caso di Hat, il livello di triptasi deve essere aggiustato

La diagnosi può essere posta in presenza di:

- criterio maggiore + 1 criterio minore

- 3 dei 4 criteri minori

Approccio multidisciplinare





ERN-EuroBloodNet

Membership

Best practices

Research

News

#ERNcare4Ua



Discomfort del paziente

- . Lungo tempo per la diagnosi
»Odissea Diagnostica»
- . Sintomi aspecifici e polidistrettuali
- . Grande impatto sulla qualità della vita



Fondamentale aumentare la consapevolezza e la conoscenza delle malattie rare nei pazienti, nella popolazione generale, **ma anche nella comunità medica**



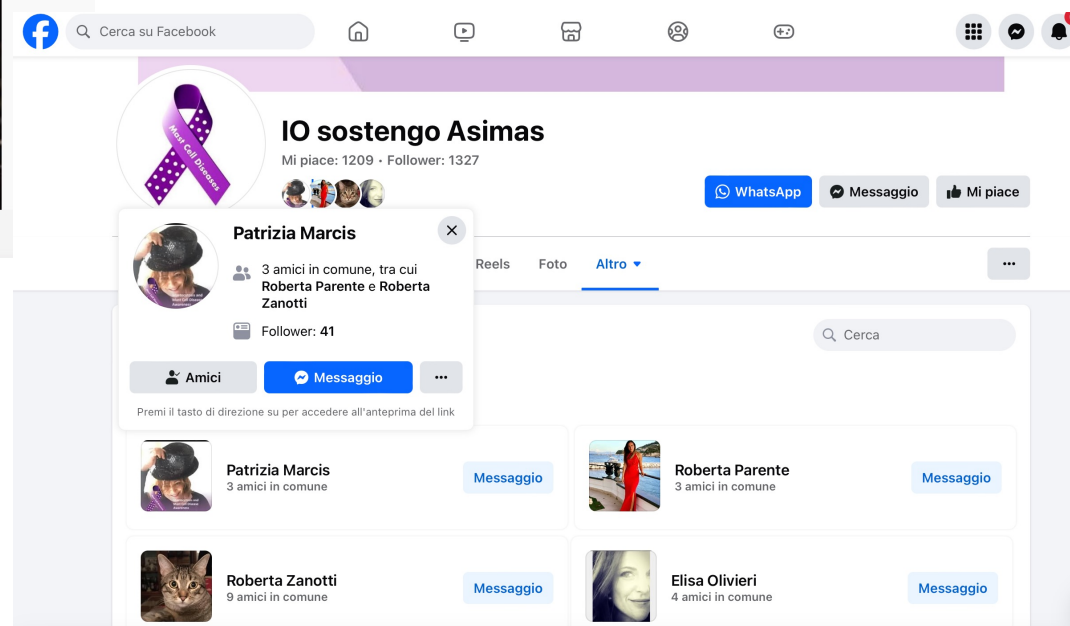
CHI SIAMO LA VOSTRA VOCE ASSOCIARSI DONAZIONI AMBULATORI NEWS MASTOCITOSI AREA UTENTI



➤attività di collaborazione con i centri di riferimento sulla Mastocitosi attraverso l'organizzazione di eventi culturali per raccogliere fondi da destinare alla ricerca

➤Obiettivo: l' inserimento della mastocitosi nell'elenco delle malattie rare esenti da ticket (codice RD0081) inserita nei nuovi LEA 2015

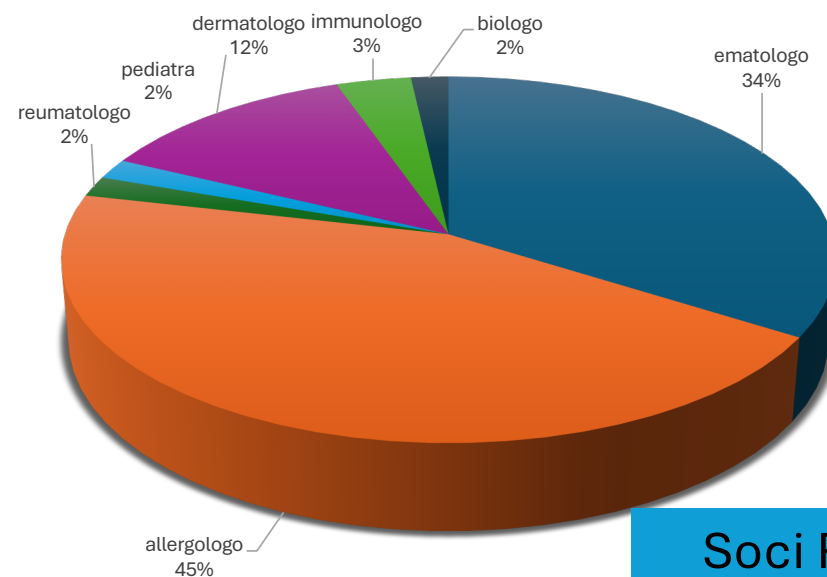
Associazione Italiana Mastocitosi
costituita nel 2008





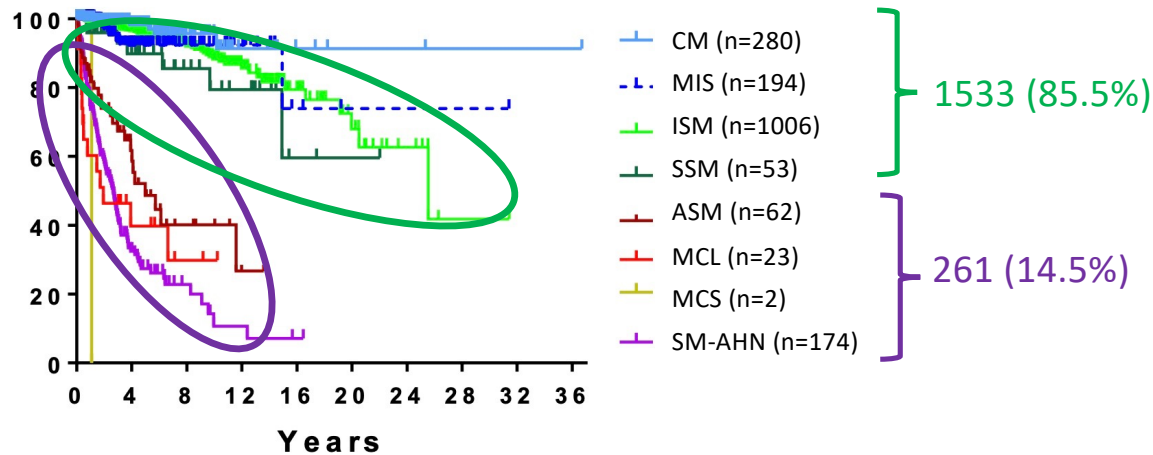
Associazione RIMA
e in Verona, via Caprera 1
93287210236

- **Promuovere la crescita di centri Multidisciplinari con livelli diagnostici e di cura il più possibile allineati con gli standard internazionali, dando quindi la possibilità ai pazienti di essere seguiti vicino a casa**



**Soci Rima
104 (87 nel
2023)**

Mastocitosi dell' adulto: Prognosi



ECNM, 2019

Non-advanced mastocytosis

OS > 90% at 10 years

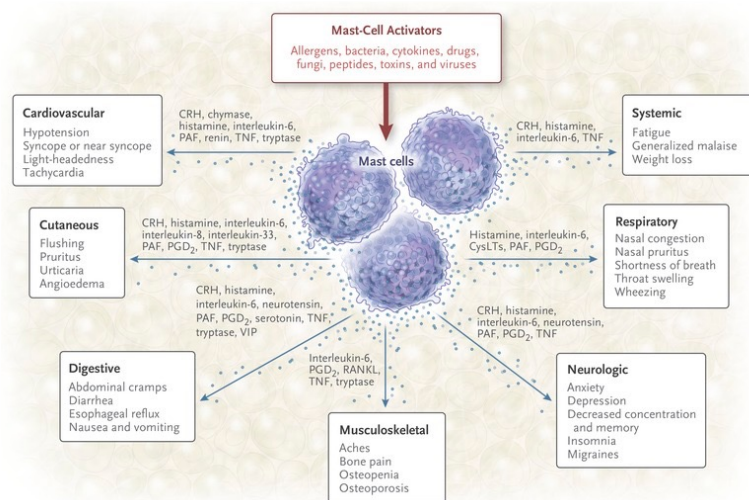
→ Control symptoms & prevent complications

Advanced mastocytosis

Median OS < 5 years

→ Reverse organ damage & improve survival

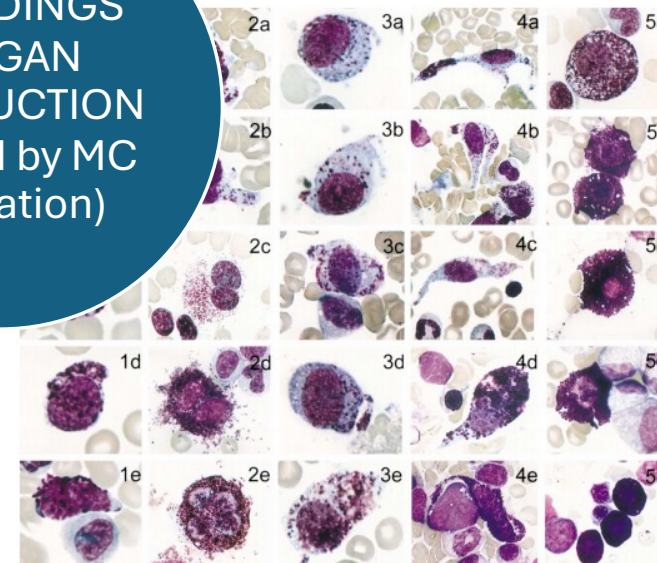
Mastocitosi: approccio terapeutico generale



Terapia anti-mediatori
Terapia sintomatica

Terapia citoriduttiva

C-FINDINGS
(ORGAN
DESTRUCTION
caused by MC
infiltration)

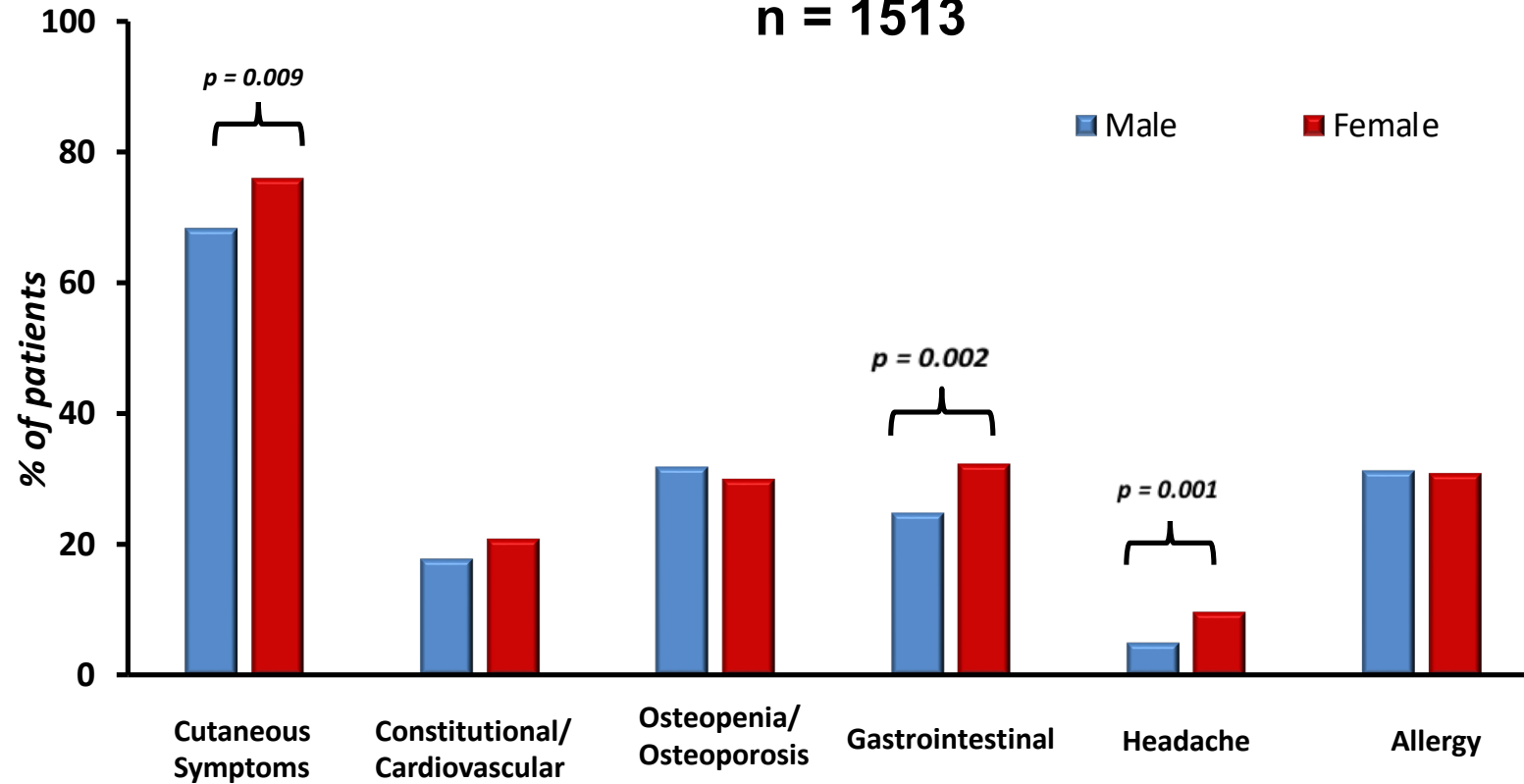


Mediator-Related Symptoms in Mastocytosis

- **Secretion of mast cell mediators is often dysregulated in patients with mastocytosis and is either dependent or independent from IgE-mediated mechanisms**
- **Mediator-related symptoms can be present in all variants of mastocytosis regardless of severity and duration of the disease**
- **They can appear at any time during the course of the disease and their spectrum and intensity can modify over time**
- **Occurrence of mediator-related symptoms is often acute and unpredictable (e.g. anaphylaxis)**
- **These symptoms are among the top concerns raised by patients and a major cause of poor quality of life in patients with mastocytosis**

Mediator-Related Symptoms in Mastocytosis (Data from the ECNM Registry – 1st Wave)

n = 1513



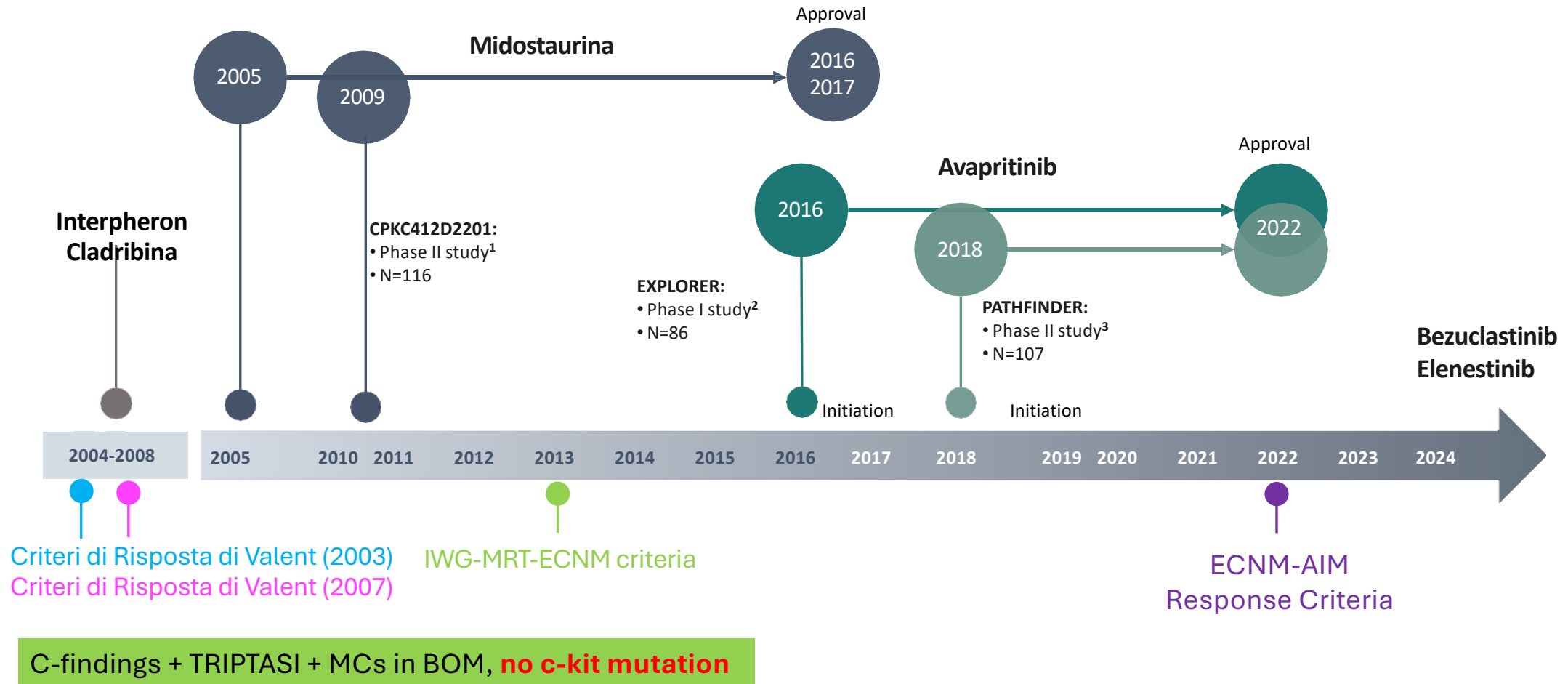
Mediator-Related Symptoms

Parente R et al., in preparation

Terapia anti-mediatori

<u>SINTOMO</u>	<u>CLASSE DI FARMACI</u>
Prurito/flushing	Anti-H1 di II generazione Anti H1 di I generazione Anti H1+stabilizzatori di membrana antileucotrienici FANS PUVA
Dolori addominali, Crampi, diarrea, nausea, gastrite	Anti H2 Inibitori di pompa Stabilizzatori di membrana Steroidi
Cefalea, difficoltà cognitive, depressione	AntiH1, anti H2 Sodio cromoglicato, antidepressivi
Episodi di ipotensione e/o anafilassi ricorrenti*	Adrenalina autoiniettabile AntiH1 + anti H2 (+ sodio cromoglicato) Immunoterapia specifica (imenotteri) Omalizumab (IgE mediati)

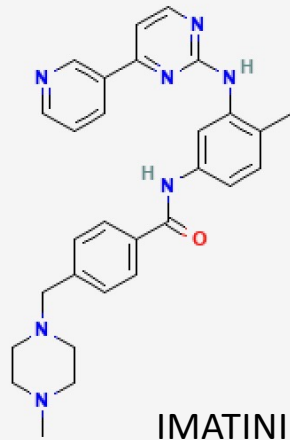
Terapia citoriduttiva



¹ Gotlib J. et al. *N Engl J Med*. 2016;374:2530-2541. ² DeAngelo DJ. et al. *Nature Med*. 2021;27:2183-2191. ³ Gotlib J. et al. *Nature Med*. 2021;27:2192-2199.

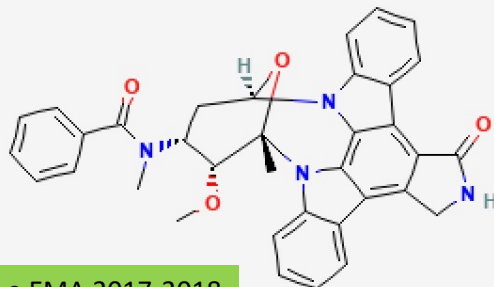
TKI in Systemic Mastocytosis

2003



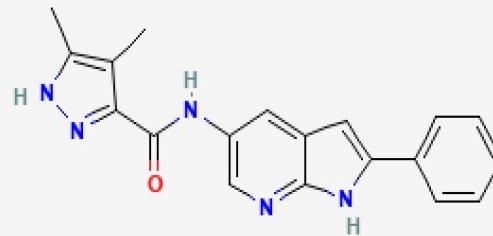
IMATINIB

IMATINIB: indicato solo nelle forme con KIT WT o varianti mutate di KIT (D560G, F522C, K509I) o riarrangiamento FIP1L1/PDGFRα
Negli altri casi riportate risposte nel 5% dei casi



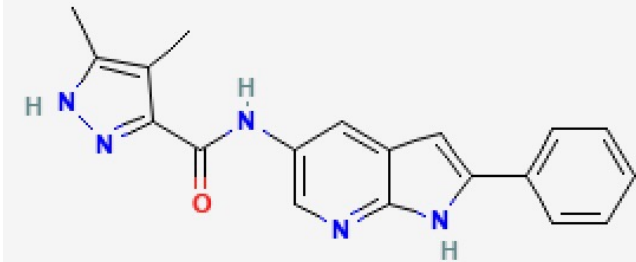
Approvato FDA e EMA 2017-2018
per Adv-SM 1° linea

MIDOSTAURIN



Trials ongoing

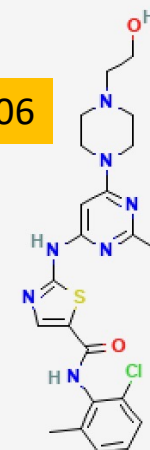
BEZUCLASTINIB



Approvato FDA e EMA 2022
per Adv-SM 2° linea

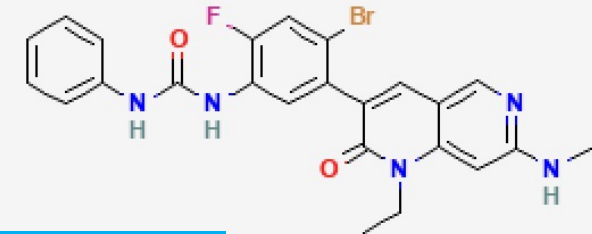
AVAPRITINIB

2006



DASATINIB

DASATINIB: efficace nel ridurre i sintomi da infiltrazione d'organo (USO)



Trials ongoing

RIPRETINIB

Midostaurin: a multitarget drug

KIT wt
KIT D816V
KIT V560G
KIT K509I
FES

FLT3 wt
FLT3 ITD
FLT3 D835H
FLT3 D835Y
FLT3 N841I
PDGFRA wt
FIP1L1-PDGfra (F/P)
F/P mutant forms
PDGFRB wt
PDGFRB mutant forms

JAK2
JAK3
AAK1
SYK
AURKA
AURKB
MARK3
PKN1
FGFR3
FGFR3 TDII (K650E)
TEL-FGFR3

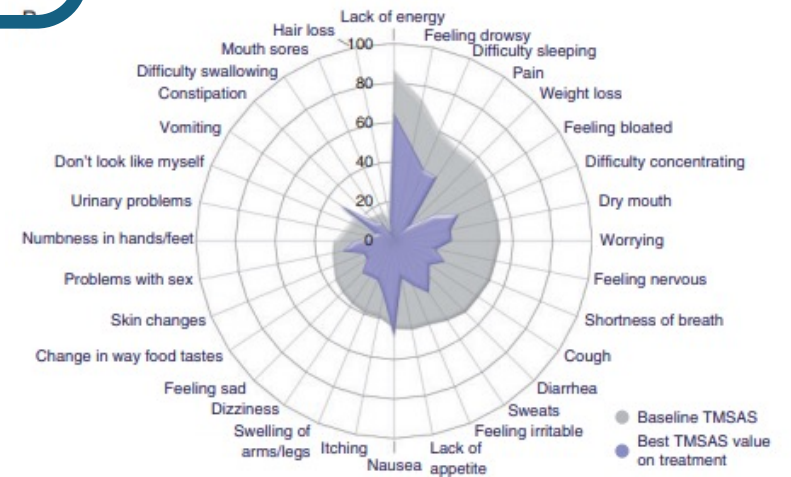


**SINGLE
AGENT
ACTIVITY:
ORR 60-69%**

**MEDIAN
DURATION OF
RESPONSE 24.1
MONTHS**

**IMPROVEMENT
OF PATIENTS-
REPORTED
SYMPTOMS**

**MANAGEABLE
TOXICITY
(GRADE 3-4:
VOMITING,
DIARRHOEA
AND FATIGUE)**



Long term efficacy of phase 2 trial A2213

AIFA 2018

Approved for treatment as monotherapy of ASM, SM-AHN and MCL patients : **100 mg x 2**

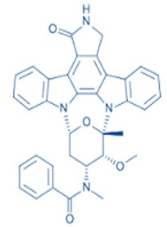


Table 1. Baseline Patient and Disease Characteristics.*

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)
KIT 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)

**116 pt
(89 evaluable)**

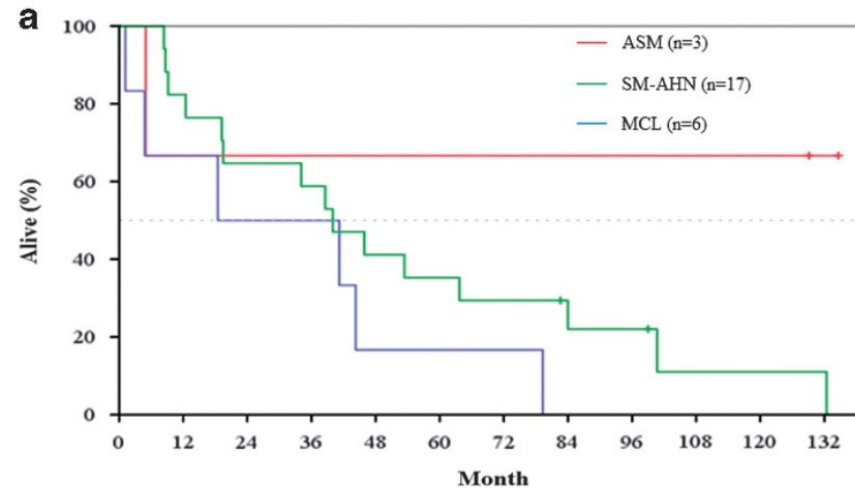
ORR 60 %

ORIGINAL ARTICLE

Efficacy and safety of midostaurin in patients with advanced systemic mastocytosis: 10-year median follow-up of a phase II trial

DJ DeAngelo¹, TI George², A Linder³, C Langford³, C Perkins³, J Ma³, P Westervelt⁴, JD Merker⁵, C Berube³, S Coutre³, M Liedtke³, B Medeiros³, D Sternberg^{6,7}, C Dutreix^{6,7}, P-A Ruffie^{6,7}, C Corless⁸, TJ Graubert⁹ and J Gotlib³

2005-2010



FU 124 mesi

ORR 69%

Gotlib, NEJM (2016)

De Angelo, Leukemia (2018)

AdvSM subtype according to MARS was predictive of median OS and TTF (CEREMAST STUDY)

170 pt

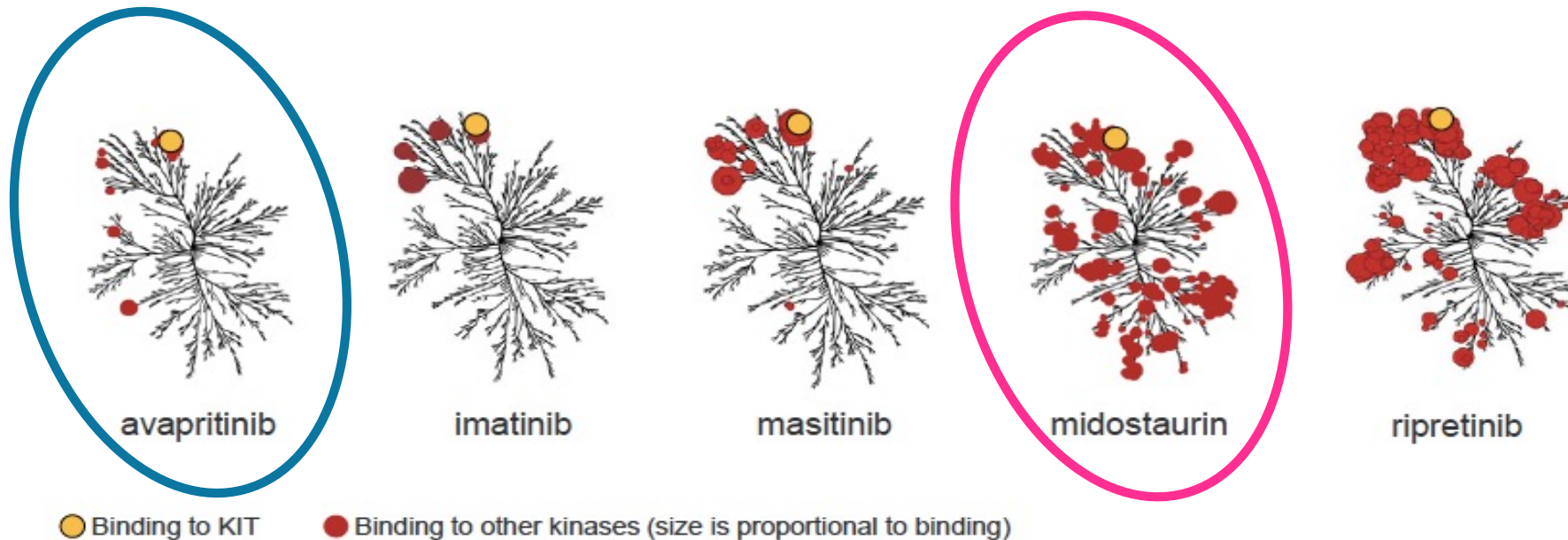
AdvSM subtype according to MARS score ^a	Median TTF, months (range)	Median OS, months (range)
Low-risk ASM	59.8 (30.5–NR)	NR (NR–NR)
Low-risk SM-AHN	26.1 (13.0–NR)	57.6 (34.4–NR)
Intermediate/high-risk ASM	6.7 (3.9–NR)	33.0 (24.4–NR)
Intermediate/high-risk SM-AHN	8.4 (5.9–12.9)	24.0 (16.9–38.2)
MCL	3.6 (3.1–NR)	9.9 (4.9–NR)

Response to treatment with midostaurin differed significantly across AdvSM subtypes (N=170; median follow-up 19 months).

Among responders (n=86), almost two-thirds (61%) discontinued midostaurin

Of these, 73% discontinued due to relapse, 23% due to intolerance, and 4% switched to allo-HSCT

Avapritinib is the only targeted therapy designed for potent and selective inhibition of the underlying driver, *KIT* D816V (and PDGFRA D842V)



<i>KIT</i> D816V biochemical IC ₅₀				
avapritinib*	imatinib*	masitinib [#]	midostaurin*	ripretinib [#]
0.27 nM	8150 nM	>1000 nM	2.9 nM	2.6 nM

PATHFINDER: Study design and patient disposition

- International, multicenter, open-label, single-arm, phase 2 study designed to assess the efficacy and safety of avapritinib in adult patients with a centrally confirmed AdvSM diagnosis

Eligibility



Centrally confirmed AdvSM diagnosis per WHO criteria



≥18 years of age



ECOG PS 0–3



Platelets $\geq 50 \times 10^9/L$

Primary endpoint:

- Centrally adjudicated ORR by mIWG-MRT-ECNM criteria

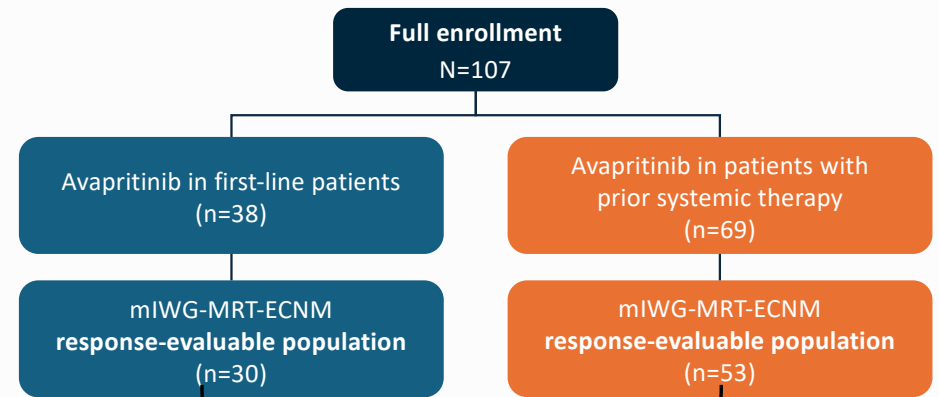
Secondary endpoints

- Biomarkers of objective disease burden measures^a
- Duration of response (DOR), progression-free survival (PFS), overall survival (OS), and safety

Exploratory endpoints

- Bone density (BD)
- Levels of bone turnover markers (PINP, TRAcP-5b)

Avapritinib 200 mg QD starting dose^b



83 pts with:

- ✓ at least 1 evaluable severe and quantifiable organ damage
- ✓ MCL regardless of C-findings

PATHFINDER: Response rate and time-to-response

IWG-MRT-ECNM

	Overall population				First-line			
	All (n=83)	ASM (n=13)	SM-AHN (n=55)	MCL (n=15)	All (n=30)	ASM (n=5)	SM-AHN (n=22)	MCL (n=3)
ORR,^a n (%)	61 (73)	10 (77)	41 (75)	10 (67)	26 (87)	4 (80)	19 (86)	3 (100)
95% CI	63–83	46–95	61–85	38–88	69–96	28–100	65–97	29–100
Best response^b								
CR or CRh^c	25 (30)	4 (31)	18 (33)	3 (20)	13 (43)	1 (20)	11 (50)	1 (33)
CR	14 (17)	1 (8)	10 (18)	3 (20)	8 (27)	1 (20)	6 (27)	1 (33)
CRh	11 (13)	3 (23)	8 (15)	0	5 (17)	0	5 (28)	0
PR ^d	32 (39)	6 (46)	19 (35)	7 (47)	13 (43)	3 (60)	8 (36)	2 (67)
CI	4 (5)	0	4 (7)	0	0	0	0	0
SD	13 (16)	3 (23)	7 (13)	3 (20)	3 (10)	1 (20)	2 (9)	0
PD	2 (2)	0	1 (2)	1 (7)	0	0	0	0
NE	7 (8)	0	6 (11)	1 (7)	1 (3)	0	1 (5)	0

median time to any response was 2.3 months (range, 0.3-20.3)

median time to CR/CRh was 9.3 months (range, 1.8-36.8).

ORR: CR+CRh+PR+CI.

^bCRh requires full resolution of all evaluable C-findings, elimination of BM mast cell aggregates, serum tryptase <20 ng/mL, resolution of palpable hepatosplenomegaly, and partial hematologic recovery (defined as absolute neutrophil count >0.5×10⁹/L with normal differential, platelet count >50×10⁹/L, and Hgb level >8.0 g/dL).

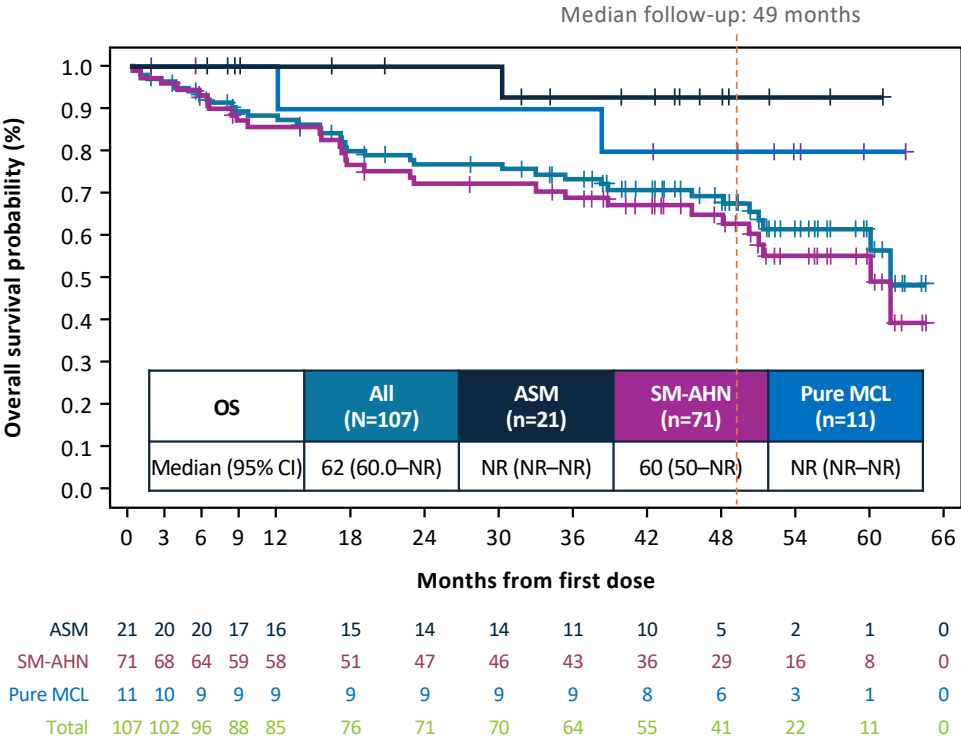
^cPR requires full resolution of ≥1 evaluable C-findings and ≥50% reduction in both BM MCs and serum tryptase.

^dTwo patients had PD as best response.

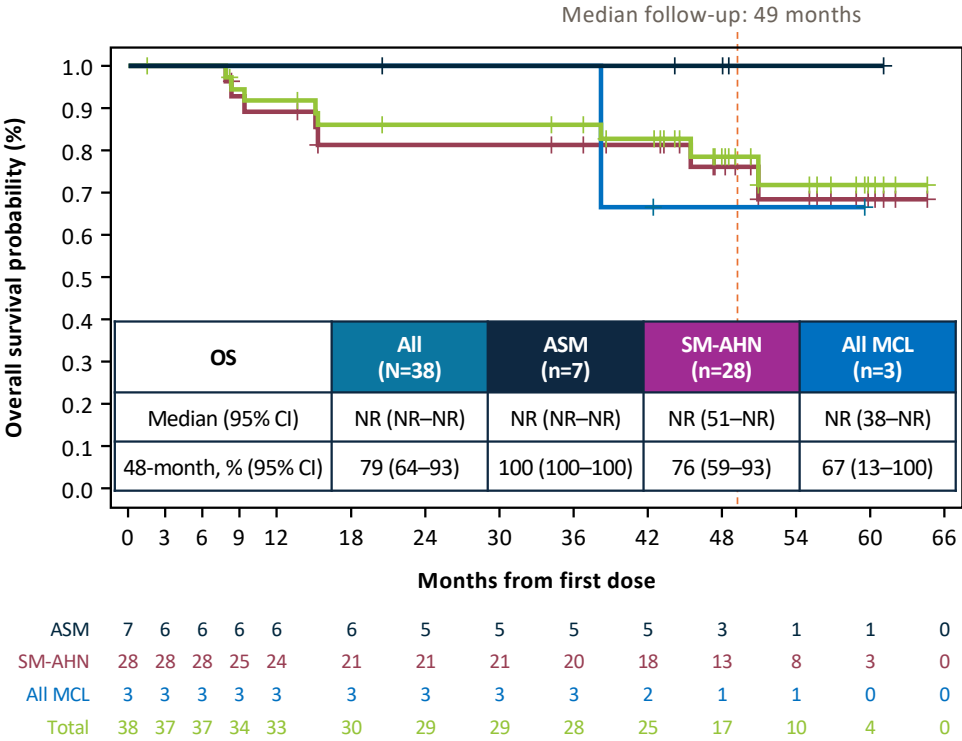
^eThe denominator is based on patients with overall response.

PATHFINDER: Update with 4 years median follow-up

OS in overall population



OS in first-line patients



- Median OS according to MARS score: not reached in low/intermediate, 48 months in high MARS score (n = 41)

Final database lock: March 13, 2025.

Reiter et al, ASH 2025
Gotlib et al, Blood Adv 2026

Tossicità Avapritinib



avapritinib

	Any-cause TEAEs*		TRAEs	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any, n (%)	107 (100)	95 (89)	103 (96)	73 (68)
Nonhematologic AEs in ≥15%, n (%)				
Periorbital edema†	61 (57)	6 (6)	59 (55)	6 (6)
Peripheral edema†	51 (48)	2 (2)	42 (39)	2 (2)
Diarrhea	38 (36)	5 (5)	16 (15)	1 (<1)
Nausea	29 (27)	1 (<1)	13 (12)	0
Arthralgia	28 (26)	2 (2)	7 (7)	0
Vomiting	25 (23)	2 (2)	9 (8)	1 (<1)
Face edema†	24 (22)	0	23 (21)	0
Fatigue	24 (22)	3 (3)	14 (13)	2 (2)
COVID-19	22 (21)	4 (4)	0	0
Epistaxis	20 (19)	0	6 (6)	0
Pruritus	19 (18)	0	5 (5)	0
Hair color changes	18 (17)	0	18 (17)	0
Rash	18 (17)	1 (<1)	7 (7)	1 (<1)
Blood alkaline phosphatase increased	17 (16)	3 (3)	9 (8)	2 (2)
Abdominal pain	16 (15)	1 (<1)	2 (2)	0
Blood creatinine increased	16 (15)	1 (<1)	3 (3)	0
Constipation	16 (15)	1 (<1)	4 (4)	0
Headache	16 (15)	0	8 (7)	0
Hematologic AEs in >15%, n (%)				
Thrombocytopenia†	62 (58)	33 (31)	55 (51)	31 (29)
Anemia†	50 (47)	25 (23)	35 (32)	17 (16)
Neutropenia†	36 (34)	32 (30)	30 (28)	27 (25)
AEs of special interest in ≥1%, n (%)				
Cognitive effects†	36 (34)	9 (8)	30 (28)	6 (6)
Cognitive disorder	21 (20)	5 (5)	19 (18)	5 (5)
Memory impairment	10 (9)	0	9 (8)	0
Confusional state	7 (7)	2 (2)	2 (2)	0
Delirium	3 (3)	2 (2)	0	0
ICB†	4 (4)	2 (2)	4 (4)	2 (2)
Subdural hematoma	2 (2)	2 (2)	2 (2)	2 (2)
Intracranial hemorrhage	2 (2)	0	2 (2)	0
AEs leading to death, n (%)	11 (10) ‡		1 (<1) §	

Efficacy and Safety of Avapritinib in Indolent Systemic Mastocytosis: Results from the Double-Blind Placebo-Controlled PIONEER Study



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DOI: [10.1056/EVIDoa2200339](https://doi.org/10.1056/EVIDoa2200339)

ORIGINAL ARTICLE

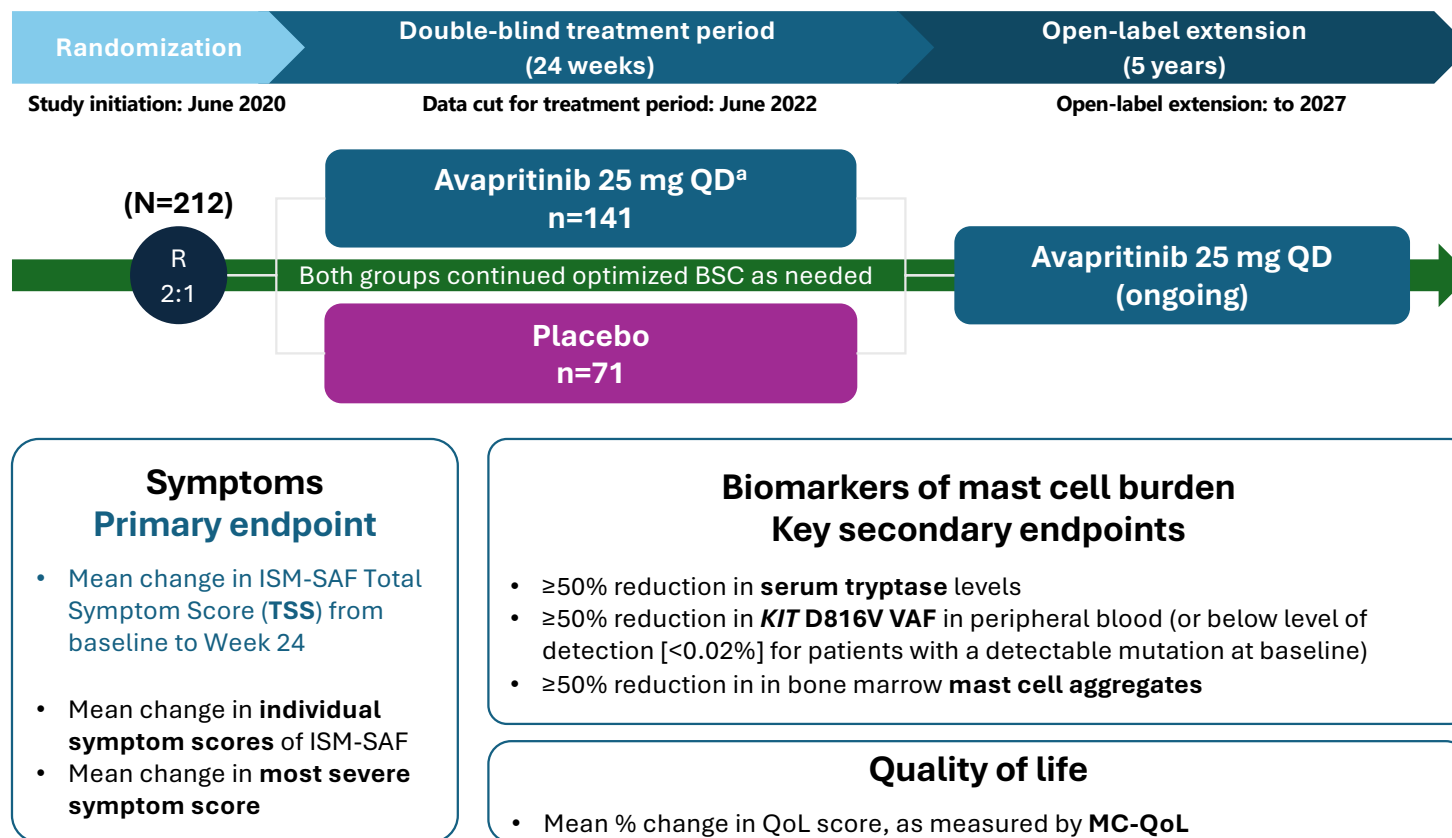
Avapritinib versus Placebo in Indolent Systemic Mastocytosis

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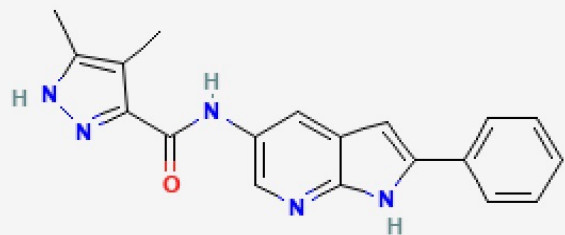
PIONEER study: Randomized, double-blind, placebo-controlled study in patients with ISM

Screening period

- Best supportive care medications (BSC) optimized for up to a month
 - Antihistamines, cromolyn, anti-IgE antibody, leukotriene receptor antagonists, corticosteroids, etc.
- Eligibility
 - Age ≥18 years
 - ISM by central pathology review
 - Moderate to severe symptoms (TSS ≥28) after ≥2 BSC medications



TKI in Indolent SM : Avapritinib



AVAPRITINIB

Approvato FDA e EMA 2022
per Adv-SM 2° linea
200 mg/ die

Potently and selectively inhibits
the autophosphorylation of KIT D816V, with an
IC₅₀ of 0.27 nanomolar in selective cellular
assays

Biochemical IC₅₀ (nM)

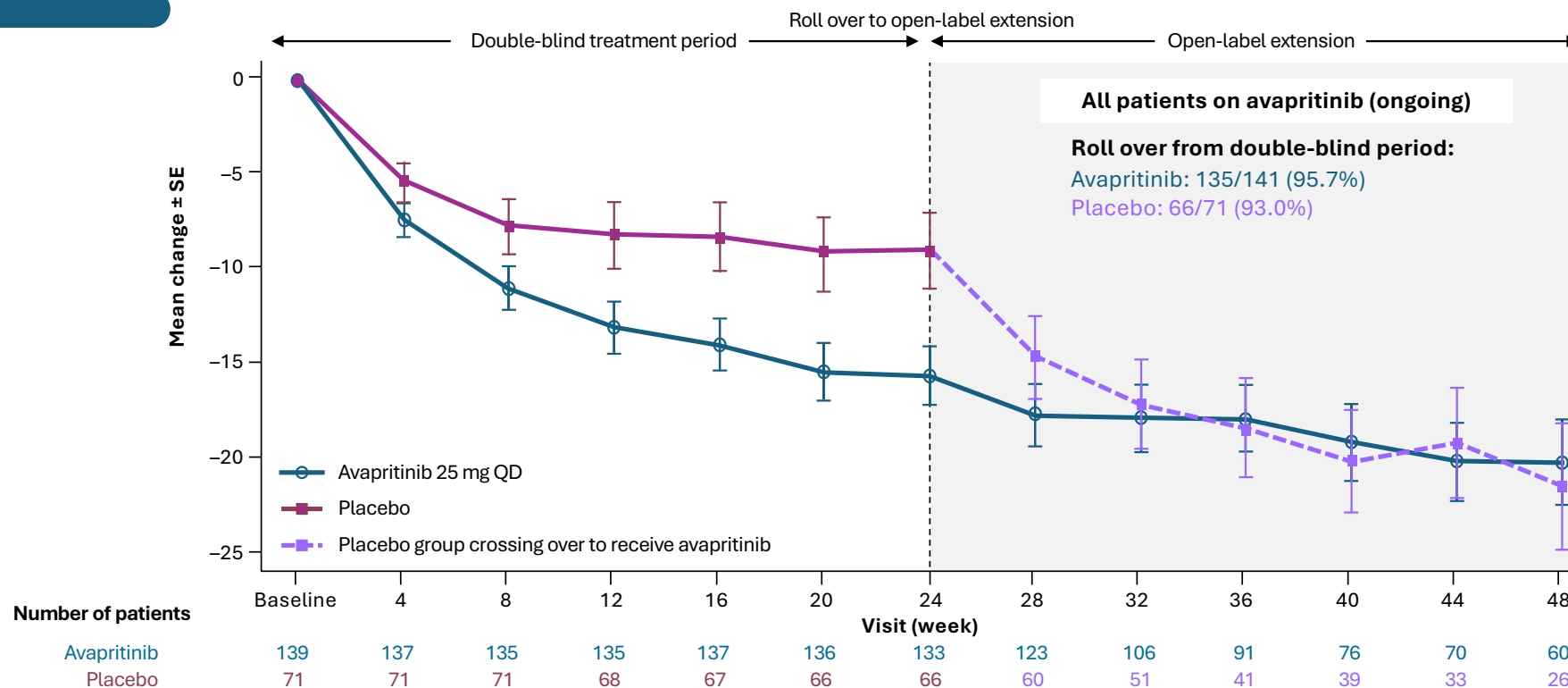
	KIT D816V	KIT wild type
Avapritinib	0.27	73

ISM Symptom Assessment Form (ISM-SAF)	
ISM Symptom	Scoring
Abdominal pain	Scored 0–10 daily on handheld device
Diarrhea	
Nausea	
Spots	0 = no symptom 10 = worst imaginable symptom
Itching	
Flushing	
Brain Fog	Analyzed as a 14-day moving average
Headache	
Dizziness	
Bone pain	
Fatigue	

- Total Symptom Score (TSS) based on severity of 11 ISM symptoms
- Score for enrollment: 28

TKI in Indolent SM : Avapritinib

TSS over time



Primary endpoint

A one-sided P-value of <0.025 was needed to declare avapritinib as superior in reducing TSS versus placebo. SE, standard error of the mean.

At Week 24	Avapritinib 25 mg QD (n=141)	Placebo (n=71)	P-value
Mean change in TSS (95% CI)	-15.58 (-18.61, -12.55)	-9.15 (-13.12, -5.18)	0.003

Avapritinib in Indolent SM safety

- Majority of AEs were Grade 1 or 2 with a low rate of discontinuation
- SAEs were reported more frequently in the placebo group (no treatment-related SAEs in either group)
- Edema adverse events were higher in the avapritinib group (majority Grade 1, and did not result in discontinuation)

	Avapritinib 25 mg QD (N=141)	Placebo (N=71)
Any AEs^{a,b}, n (%)	128 (90.8)	66 (93.0)
Grade 1–2 AEs	98 (69.5)	51 (71.8)
Grade 1–2 related AEs	74 (52.5)	30 (42.3)
Grade ≥3 AEs	30 (21.3)	15 (21.1)
Grade ≥3 related AEs	3 (2.1)	2 (2.8)
SAEs, n (%)	7 (5.0)	8 (11.3)
Any grade TRAEs	77 (54.6)	32 (45.1)
Most frequently reported TRAEs (≥5% of patients)		
Headache	11 (7.8)	7 (9.9)
Nausea	9 (6.4)	6 (8.5)
Peripheral edema	9 (6.4)	1 (1.4)
Periorbital edema	9 (6.4)	2 (2.8)
Dizziness	4 (2.8)	5 (7.0)
TRAEs leading to discontinuation	2 (1.4)	1 (1.4)

A Phase 2/3 Study of BLU-263, a Highly Potent and Selective Tyrosine Kinase Inhibitor, in Patients With Indolent Systemic Mastocytosis (ISM) and Monoclonal Mast Cell Activation Syndrome (mMCAS)

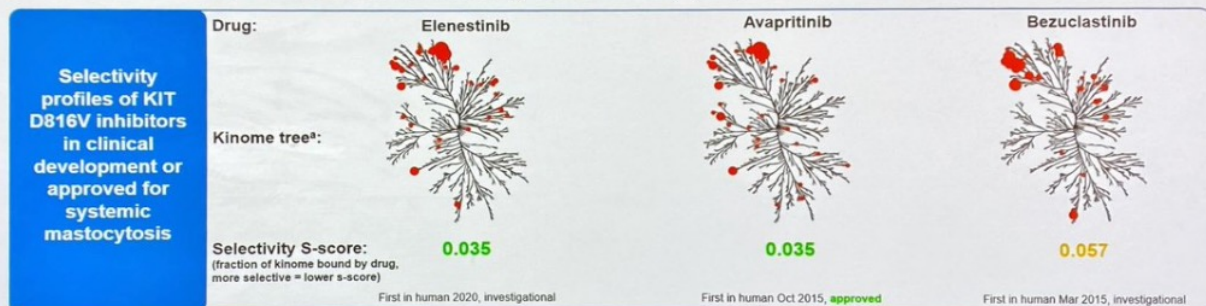
Elenestinib (BLU-263): A next-generation, potent, selective KIT D816V inhibitor

- Elenestinib is a novel, investigational, oral, next-generation tyrosine kinase inhibitor that is non-brain penetrant^{1,2}

- Potently and selectively inhibits KIT D816V while preferentially sparing wild-type KIT

- Well-characterized product formulation allowing for once-daily (QD) dosing^{1,2}

	KIT D816V phosphorylation IC ₅₀	WT KIT proliferation IC ₅₀	WT KIT phosphorylation IC ₅₀
Elenestinib	3.1 nM	95.9 nM	82.6 nM
Avapritinib	3.1 nM	85.8 nM	89.5 nM
Bezacastinib	3.4 nM	26.4 nM	32.5 nM



IC₅₀, half-maximal inhibitory concentration; QD, once daily; WT, wild-type.

1. Dave N et al. Presented at AACR 2021. Poster #CT122; 2. Castells M et al. Presented at EHA 2022. Poster #1017

^aKinome illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com) (CSTI). The foregoing website is maintained by CSTI and Blueprint Medicines is not responsible for its content.

Primary endpoints	Secondary endpoints
Part 1 - Determination of RD - PK and PD Part 2 - Proportion of patients who achieve a ≥ 30% reduction in ISM-SAF TSS from baseline at Week 25 Parts 1 and 3 - Safety and tolerability - Mean change in ISM-SAF TSS^{a,c}	Part 1 - Mean change in ISM-SAF Individual Symptom Scores^a Part 2 ≥ 50% reduction in measures of MC burden^b - Mean change in ISM-SAF Parts 1 and 2 - Mean change in measures of MC burden^{a,b} Part 3 - Mean change in serum tryptase and KIT D816V VAF in the blood^c - Mean change in ISM-SAF Individual and Lead Symptom Scores from baseline

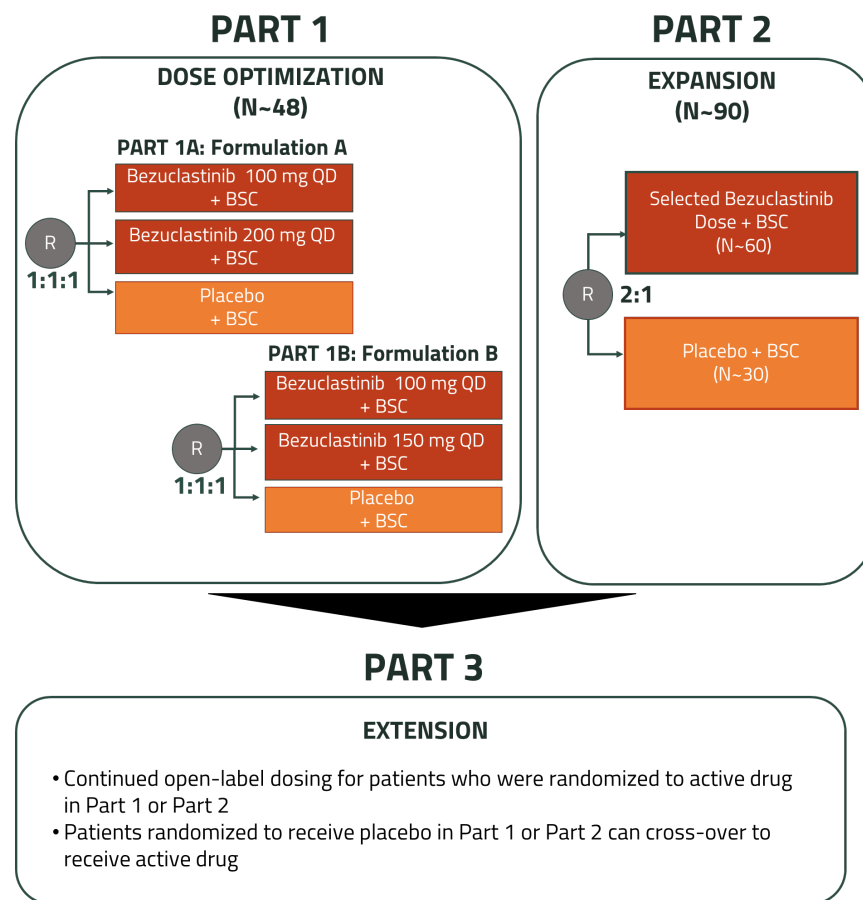
Current study sites

- Australia
- Austria
- Belgium
- France
- Germany
- Italy
- Netherlands
- Portugal
- Spain
- Switzerland
- UK
- USA
- Denmark

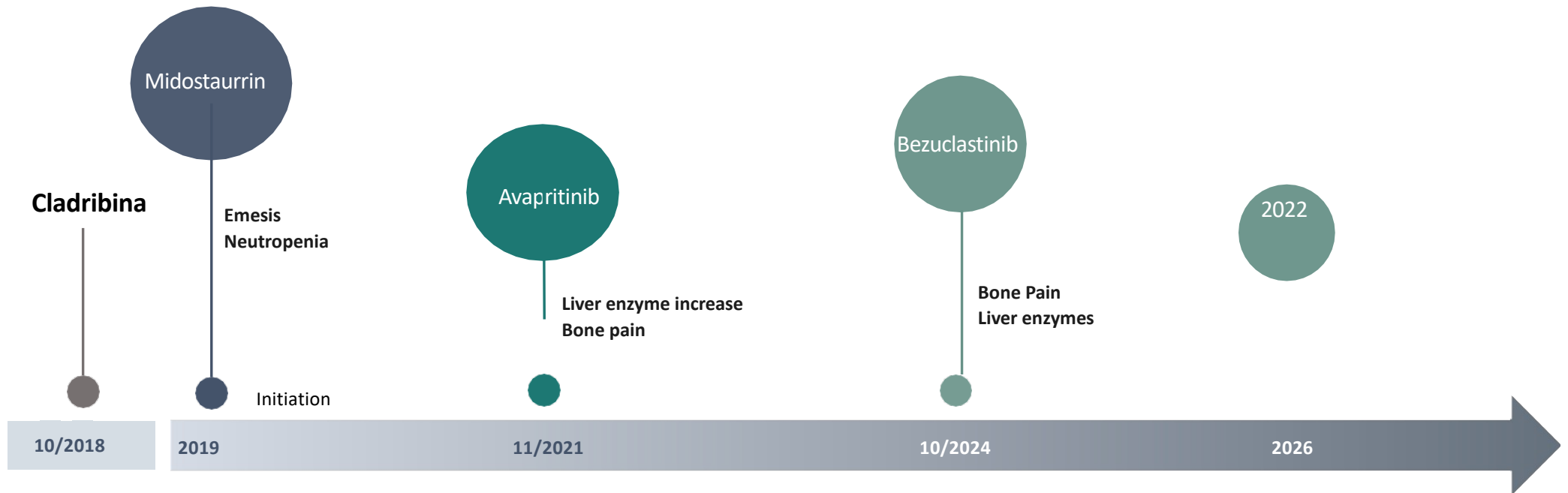


Summit: A Multi-Part, Randomized, Double-Blind, Placebo-Controlled Phase 2 Clinical Study of the Safety and Efficacy of Bezucastinib in Patients with Indolent and Smoldering SM

Study Design



TOXICITY CASE



09/2018 Diagnosis of ASM

Excellent Remission achieved with all three TKIs...
But Adverse Events Grade III on all drugs...

Conclusioni

- . La Mastocitosi Sistemica continua ad essere una malattia spesso di difficile diagnosi e riconoscimento
- . L'aspetto multidisciplinare è fondamentale
- . Lo scenario terapeutico delle mastocitosi sistemiche è in rapida evoluzione, mirato anche al controllo dei sintomi delle forme indolenti
- . La terapia delle forme indolenti modifica la prospettiva di valutazione di risposta dove l'obiettivo è il controllo dei sintomi, e non la sopravvivenza
- . Saranno necessari nuovi strumenti di "quantificazione" dei sintomi per un utilizzo razionale dei farmaci nel setting delle ISM



Patrizia Bonadonna, Roberta Zanotti, Federica Grifoni, Simona Soverini, Cristina Papayannidis, Chiara Elena,
Massimiliano Bonifacio, Luigi Scaffidi, Roberta Parente, Massimo Triggiani, Francesco Mannelli, Patrizia Marcis e Paolo Camaggi
(Verona, Milano, Bologna, Ravenna, Pavia, Napoli, Firenze)