



Online Repository Figure E1 (ECNM and GREM). Patient flow diagram.

Abbreviations: AdvSM, advanced systemic mastocytosis; AP, alkaline phosphatase; ASM, aggressive systemic mastocytosis; β2-MG, β2-microglobuline; BMM, bone marrow mastocytosis; ECNM, European Competence Network on Mastocytosis; GREM, German Registry on Eosinophils and Mast Cells; ISM, indolent systemic mastocytosis; MCL, mast cell leukemia; SM-AHN, systemic mastocytosis with an associated hematologic neoplasm; SSM, smoldering systemic mastocytosis.

Online Repository Table E1. Demographic and disease characteristics of 2607 SM patients enrolled within the ECNM.

	ISM	BMM	SSM	ASM	SM-AHN	MCL
Number of patients, n (%)	1734 (66)	327 (13)	58 (2)	117 (4)	326 (13)	45 (2)
Age at diagnosis; median (range)	47 (5-82)	53 (19-83)	57 (29-79)	60 (16-83)	66 (20-87)	54 (27-90)
Male, n (%)	684/1734 (39)	208/327 (64)	23/58 (40)	68/117 (58)	226/326 (69)	26/45 (58)
C-findings						
Hemoglobin, g/dL; median (range)	14 (10-18)	15 (10-18)	13 (10-17)	11 (4-17)	11 (4-18)	10 (7-15)
<10g/dL, n (%)	0/1591 (0)	0/316 (0)	0/57 (0)	37/108 (34)	106/319 (33)	20/45 (44)
Platelets, x10 ⁹ /L; median (range)	265 (30-930)	245 (99-589)	214 (75-581)	176 (5-681)	125 (5-969)	214 (75-581)
<100x10 ⁹ /L, n (%)	0/1591 (0)	0/316 (0)	0/57 (0)	34/108 (32)	139/319 (44)	22/45 (49)
ANC, x10 ⁹ /L; median (range)	4 (0-15)	4 (0-42)	4 (1-22)	4 (0-26)	5 (0-86)	5 (1-76)
<1x10 ⁹ /L, n (%)	0/1513 (0)	0/310 (0)	0/50 (0)	7/98 (7)	15/306 (5)	1/42 (2)
Alkaline phosphatase, U/L; median (range)	72 (28-317)	67 (22-142)	138 (44-517)	186 (20-1696)	159 (39-1407)	147 (55-989)
>150U/L, n (%)	40/1289 (3)*	0/276 (0)	20/47 (43)	59/95 (62)	149/288 (52)	19/40 (48)
Albumin level, g/L; median (range)	45 (28-57)	44 (32-53)	44 (34-54)	39 (18-52)	39 (16-57)	37 (25-54)
<34g/L, n (%)	8/1112 (1)*	1/247 (0)*	0/34 (0)	19/77 (25)	57/269 (21)	9/34 (27)
Ascites, n (%)	4/1546 (0)*	0/313 (0)	0/53 (0)	36/101 (36)	83/281 (30)	11/41 (27)
Portal hypertension, n (%)	3/1532 (0)*	1/314 (0)*	2/52 (4)*	16/95 (17)	30/245 (12)	2/33 (6)
Weight loss (>10 % over last 6 months), n (%)	20/1622 (1)*	1/320 (0)*	2/57 (4)*	65/109 (60)	136/307 (44)	22/39 (56)
Osteolytic lesions, n (%)	11/1405 (1)*	1/298 (0)*	1/48 (2)*	30/99 (30)	15/238 (6)	4/32 (13)
B-findings						
Dysmyelopoiesis, n (%)	19/1593 (1)	1/316 (0)	13/54 (24)	42/96 (44)	217/304 (71)	23/42 (55)
MC-infiltration in BM biopsy, %; median (range)	10 (0-85)	5 (1-40)	40 (15-90)	30 (1-95)	20 (0-95)	75 (20-90)
Serum tryptase level, µg/L; median (range)	32 (1-885)	21 (2-366)	202 (3-2100)	171 (9-1432)	135 (2-4980)	308 (75-4530)
Serum tryptase level, ≥125µg/L, n (%)	138/1639 (8)	9/325 (3)	49/56 (88)	66/110 (60)	155/290 (53)	39/41 (95)
Splenomegaly, n (%)	77/1639 (5)	5/320 (2)	44/58 (76)	69/113 (61)	194/303 (64)	32/42 (76)
Hepatomegaly, n (%)	91/1634 (6)	13/318 (4)	33/58 (57)	60/112 (54)	148/300 (49)	23/42 (55)
Lymphadenopathy, n (%)	26/1536 (2)	6/314 (2)	15/49 (31)	40/98 (41)	106/248 (43)	9/34 (27)
Other relevant findings						
Leukocytes, x10 ⁹ /L; median (range)	6.5 (1.0-18.5)	6.4 (1.0-67.0)	6.3 (2.3-30.1)	6.9 (1.2-38.9)	9.3 (0.6-12.9)	8.4 (2.0-97.3)
Monocytes, x10 ⁹ /L; median (range)	0.4 (0.0-3.6)	0.4 (0.0-4.0)	0.3 (0.0-2.1)	0.5 (0.0-5.7)	0.9 (0.0-18.7)	0.5 (0.1-6.8)
Eosinophils, x10 ⁹ /L; median (range)	0.1 (0.0-7.5)	0.1 (0.0-2.9)	0.1 (0.0-7.5)	0.2 (0.0-1.8)	0.2 (0.0-18.5)	0.3 (0.0-35.0)
<i>KIT</i> D816V positivity, n (%)	1229/1425 (86)	250/287 (87)	41/42 (98)	88/96 (92)	258/291 (89)	25/39 (64)
β2-microglobulin, ≥2.5mg/L, n (%)	25/317 (8)	7/117 (6)	4/12 (33)	22/29 (76)	61/78 (78)	8/12 (67)
LDH, ≥260 U/L; n (%)	96/1223 (8)	39/264 (15)	3/49 (6)	11/99 (11)	77/276 (28)	10/40 (25)
Outcome						
Follow-up since diagnosis, median (range)	2.0 (0.0-28.7)	2.3 (0.0-19.5)	6.2 (1.0-17.4)	2.5 (0.0-17.4)	1.5 (0.0-15.6)	1.0 (0.0-10.0)
Lost to follow-up, n	1390 (80)	268 (82)	44 (76)	62 (53)	142 (44)	16 (36)
Deaths, n (%)	47/1258 (4)	6/219 (3)	6/49 (12)	39/101 (39)	169/285 (59)	25/41 (61)

Abbreviations: ANC, absolute neutrophil count; ASM, aggressive systemic mastocytosis; BMM, bone marrow mastocytosis; ISM, indolent systemic mastocytosis; MCL, mast cell leukemia; SM-AHN, systemic mastocytosis with an associated hematological neoplasm; SSM, smoldering systemic mastocytosis. * Not assessed as SM related C-findings.

Online Repository Table E2. Demographic and disease characteristics of 685 SM patients with available outcome data enrolled within the ECNM.

	ISM	BMM	SSM	ASM	SM-AHN	MCL
Number of patients, n (%)	344 (50)	59 (9)	14 (2)	55 (8)	184 (27)	29 (4)
Age at diagnosis; median (range)	45 (17-81)	49 (22-79)	56 (29-76)	64 (21-83)	67 (22-87)	58 (27-90)
Male, n (%)	162/344 (47)	34/59 (58)	5/14 (36)	40/55 (73)	137/184 (73)	15/29 (52)
C-findings						
Hemoglobin, g/dL; median (range)	14 (10-18)	15 (11-18)	13 (10-16)	10 (4-16)	10 (6-16)	10 (7-13)
<10g/dL, n (%)	0/320 (0)	0/54 (0)	0/14 (0)	26/52 (50)	77/179 (43)	15/29 (52)
Platelets, x10 ⁹ /L; median (range)	258 (100-930)	250 (100-589)	209 (100-405)	116 (5-681)	94 (0-969)	87 (16-305)
<100x10 ⁹ /L, n (%)	0/320 (0)	0/54 (0)	0/14 (0)	20/52 (39)	95/179 (53)	17/29 (59)
ANC, x10 ⁹ /L; median (range)	4 (0-15)	4 (0-10)	5 (2-22)	4 (0-26)	5 (0-80)	5 (1-13)
<1x10 ⁹ /L, n (%)	0/302 (0)	0/50 (0)	0/10 (0)	6/49 (12)	8/172 (5)	1/27 (4)
Alkaline phosphatase, U/L; median (range)	80 (35-317)	73 (39-142)	143 (75-212)	218 (47-1696)	214 (39-1279)	148 (55-539)
>150U/L, n (%)	21/270 (8)*	0/46 (0)	4/10 (40)*	35/47 (75)	103/167 (62)	12/25 (48)
Albumin level, g/L; median (range)	45 (29-55)	45 (32-53)	48 (38-53)	35 (18-49)	38 (16-54)	37 (25-43)
<34g/L, n (%)	2/241 (1)*	1/40 (3)*	0/5 (0)	14/42 (33)	46/158 (29)	7/32 (2)
Ascites, n (%)	1/307 (0)*	0/55 (0)	0/12 (0)	21/45 (47)	56/159 (35)	8/27 (30)
Portal hypertension, n (%)	1/302 (0)*	0/56 (0)	0/11 (0)	8/42 (19)	24/137 (18)	2/22 (9)
Weight loss (>10 % over last 6 months), n (%)	1/324 (0)*	0/56 (0)	0/14 (0)	37/53 (70)	100/175 (57)	14/24 (58)
Osteolytic lesions, n (%)	0/287 (0)	1/53 (2)*	3/14 (21)*	25/46 (54)	144/175 (82)	17/27 (63)
B-findings						
Dysmyelopoiesis, n (%)	5/321 (2)	1/53 (2)	3/14 (21)	25/46 (54)	144/175 (82)	17/27 (63)
MC-infiltration in BM biopsy, %; median (range)	10 (0-50)	5 (1-20)	33 (15-90)	30 (1-95)	30 (2-95)	80 (20-100)
Serum tryptase level, µg/L; median (range)	42 (3-885)	30 (4-366)	179 (60-486)	200 (9-1432)	173 (2-1022)	416 (114-4530)
Serum tryptase level, >125µg/L, n (%)						
Splenomegaly, n (%)	23/327 (7)	0/55 (0)	12/14 (86)	35/52 (67)	124/175 (71)	22/27 (82)
Hepatomegaly, n (%)	21/324 (7)	0/55 (0)	9/14 (64)	31/51 (61)	103/173 (60)	14/27 (52)
Lymphadenopathy, n (%)	3/297 (1)	2/54 (4)	3/10 (30)	16/41 (39)	74/141 (53)	6/22 (27)
Other relevant findings						
Leukocytes, x10 ⁹ /L; median (range)	6.6 (1.0-15.0)	7.0 (1.9-15.0)	6.9 (3.6-30.1)	6.9 (1.4-38.9)	10.0 (0.6-111.7)	9.5 (2.0-53.3)
Monocytes, x10 ⁹ /L; median (range)	0.4 (0.0-3.0)	0.4 (0.0-1.1)	0.2 (0.0-2.1)	0.4 (0.0-5.7)	1.0 (0.0-18.7)	0.5 (0.0-2.0)
Eosinophils, x10 ⁹ /L; median (range)	0.1 (0.0-3.4)	0.2 (0.0-1.1)	0.2 (0.0-1.8)	0.2 (0.0-18.5)	0.3 (0.0-35.0)	0.1 (0.0-5.9)
<i>KIT</i> D816V positivity, n (%)	217/261 (83)	30/44 (68)	10/10 (100)	36/41 (88)	143/158 (91)	13/25 (52)
β2-microglobulin, ≥2.5mg/L, n (%)	7/80 (9)	7/59 (12)	2/5 (40)	10/13 (77)	28/35 (80)	6/8 (75)
LDH, ≥260 U/L; n (%)	17/256 (7)	7/41 (17)	1/10 (10)	8/49 (16)	51/151 (34)	9/26 (35)
Outcome						
Follow-up since diagnosis, median (range)	2.0 (0.0-28.6)	2.3 (0.0-19.9)	6.2 (1.0-17.4)	2.5 (0-17.4)	1.5 (0.0-15.6)	1.0 (0.0-10.1)
Deaths, n (%)	47/344 (14)	6/59 (10)	6/14 (43)	39/55 (71)	166/184 (90)	25/29 (86)

Abbreviations: ANC, absolute neutrophil count; ASM, aggressive systemic mastocytosis; BMM, bone marrow mastocytosis; ISM, indolent systemic mastocytosis; MCL, mast cell leukemia; SM-AHN, systemic mastocytosis with an associated hematological neoplasm; SSM, smoldering systemic mastocytosis. * Not assessed as SM related C-findings.

Online Repository Table E3. 1,951 patients with systemic mastocytosis (ECNM) stratified according to LDH \geq / $<$ 260U/L.

	LDH \geq 260U/L		LDH $<$ 260U/L	
	Presence of AHN	Absence of AHN	Presence of AHN	Absence of AHN
Number of patients at diagnosis, n (%)	77 (33)	159 (67)	199 (12)	1516 (88)
Age in years; median (range)	63 (28-83)	50 (18-90)	67 (19-87)	48 (5-83)
Male, n (%)	57/77 (74)	92/159 (58)	133/199 (67)	656/1516 (43)
C-Findings				
Hemoglobin, g/dL; median (range)	11 (4-17)	14 (6-18)	11 (7-18)	14 (4-18)
<10g/dL, n (%)	31/77 (40)	13/156 (8)	62/196 (32)	45 (1496)
Platelets, $\times 10^9$ /L; median (range)	103 (0-958)	239 (16-930)	120 (12-893)	258 (5-681)
<100 $\times 10^9$ /L, n (%)	38/77 (49)	13/156 (8)	86/196 (44)	55/1496 (4)
ANC, $\times 10^9$ /L; median (range)	7 (0-86)	4 (0-19)	3.8 (0.1-72.2)	3.9 (0.0-75.9)
<1 $\times 10^9$ /L, n (%)	5/75 (7)	2/147 (1)	7/192 (4)	13/1432 (1)
Alkaline phosphatase, U/L; median (range)	135 (39-1010)	74 (34-1696)	177 (47-1407)	74 (20-989)
>150U/L, n (%)	36/76 (47)	22/127 (16)	102/189 (54)	104/1416 (7)
Albumin level, g/L; median (range)	38 (16-54)	42 (18-55)	40 (21-54)	44 (20-57)
<34g/L, n (%)	16/66 (24)	10/122 (8)	33/177 (19)	25 (2)
Ascites, n (%)	15/71 (21)	8/156 (5)	61/180 (34)	36/1421 (3)
Portal hypertension, n (%)	5/64 (8)	2/153 (1)	22/155 (14)	20/1403 (1)
Weight loss (>10 % over last 6 months), n (%)	30/75 (40)	14/156 (9)	90/189 (48)	82/1465 (6)
Osteolytic lesions, n (%)	4/59 (7)	3/147 (2)	11/157 (7)	36/1301 (3)
B-Findings				
Dysmyelopoiesis, n (%)	55/72 (76)	9/157 (6)	132/184 (72)	74/1425 (5)
BM MC infiltration, %; median (range)	15 (1-90)	10 (0-100)	30 (0-95)	10 (0-100)
Serum tryptase level, μ g/L; median (range)	129 (6-673)	34 (1-4530)	149 (2-4980)	32 (3-2100)
>125 μ g/L, n (%)	35/67 (52)	24/153 (16)	105/188 (56)	225 (15)
Splenomegaly, n (%)	42/73 (58)	23/158 (15)	131/191 (69)	160/1481 (11)
Hepatomegaly, n (%)	37/75 (49)	21/159 (13)	93/186 (50)	156/1476 (11)
Lymphadenopathy, n (%)	22/60 (37)	10/150 (7)	75/163 (46)	73/1402 (5)
Other relevant findings				
Leukocytes, $\times 10^9$ /L; median (range)	15.0 (0.0-129.3)	6.7 (1.1-53.3)	7.7 (1.0-83.0)	6.6 (1.0-97.3)
>16.000 $\times 10^9$ /L, n (%)	36/77 (47)	11/157 (7)	37/198 (19)	18/1495 (1)
Monocytes, $\times 10^9$ /L; median (range)	0.5 (0.0-18.7)	0.4 (0.0-8.2)	0.8 (0.0-8.2)	0.4 (0.0-6.8)
>0.8 $\times 10^9$ /L	44/76 (58)	16/132 (12)	96/190 (51)	95/1406 (7)
Eosinophils, $\times 10^9$ /L; median (range)	0.4 (0.0-35.0)	0.1 (0.0-3.5)	0.2 (0.0-13.3)	0.1 (0.0-18.5)
>1.5 $\times 10^9$ /L	17/73 (23)	6/136 (4)	33/184 (18)	24/1402 (2)
<i>KIT</i> D816V positive, n (%)	58/68 (85)	105/131 (80)	166/186 (89)	1142/1309 (87)
BM MC burden in smears, %; median (range)	5 (0-30)	5 (0-80)	7 (1-80)	1 (0-100)
Outcome				
Follow-up, years, median (range)	1.3 (0.1-9.2)	2.4 (0.0-22.3)	1.9 (0.0-15.6)	2.1 (0.0-28.6)
Death, n (%)	47/72 (65)	18/145 (12)	93/165 (56)	84/1071 (8)

Abbreviations: ANC, absolute neutrophil count; AHN, associated hematologic neoplasm; BM, bone marrow; GI, gastrointestinal; MC, mast cell; NS., not significant