## Chronic myelomonocytic leukemia: molecular pathogenesis and therapeutic innovations

Ludovica Marando, Clifford M. Csizmar and Mrinal M. Patnaik

Division of Hematology, Department of Internal Medicine, Mayo Clinic, MN, USA.

Correspondence: L. Marando Marando.Ludovica@mayo.edu

M.M. Patnaik

Patnaik.Mrinal@mayo.edu

**Received:** June 12, 2024. Accepted: October 4, 2024. Early view: October 17, 2024.

https://doi.org/10.3324/haematol.2024.286061

©2025 Ferrata Storti Foundation Published under a CC BY-NC license



Supplementary Table 1. Demographics of the Mayo Clinic CMML Cohort CMML Cohort dCMML Variable **Format DCMML** 391 750 355 **Demographics** 71 (18 - 95) 71 (27 - 95) 70 (18 - 91) Age Median (range) Number (%) 280 (71.6%) Male 501 (66.8%) 221 (62.3%) Number (%) Female 249 (33.2%) 111 (28.4%) 134 (37.7%) **Laboratory Parameters** Hemoglobin (g/dL) 10.8 (4.2 - 16.9) 10.9 (6.4 - 16.8) 10.8 (4.2 - 16.9) Median (range) Mean Corpuscular Volume (MCV, fL) 92.0 (70.3 - 124.9) Median (range) 92.0 (59.0 - 124.9) 92.1 (59.0 - 124.3) Median (range) 98 (6 - 742) Platelet Count (x109/L) 99 (6 - 1277) 104 (7 - 1277) White Blood Cell Count (WBC, x109/L) 12.3 (1.3 - 264.8) 7.1 (1.3 - 12.9) 25.1 (13.0 - 264.8) Median (range) Absolute Neutrophil Count (ANC, x109/L) 5.9 (0.0 - 151.0) 3.1 (0.0 - 14.1) 14.0 (1.4 - 151.0) Median (range) Absolute Monocyte Count (AMC, x109/L) Median (range) 2.5 (0.0 - 87.4) 1.5 (0.0 - 9.2) 5.3 (0.1 - 87.4) Absolute Lymphocyte Count (ALC, x109/L) Median (range) 1.8 (0.0 - 22.0) 1.5 (0.3 - 6.2) 2.6 (0.0 - 22.0) Immature Myeloid Cells (IMC) Present Number (%) 431 (58.5%) 159 (41.1%) 272 (77.7%) Peripheral Blood Blasts (%) Median (range) 0 (0 - 19) 0 (0 - 17) 0 (0 - 19) Bone Marrow Blasts (%) Median (range) 3 (0 - 19) 3 (0 - 19) 3 (0 - 19) **FAB Subtype** Dysplastic Number (%) 391 (52.4%) 391 (100%) 0 (0%) Proliferative Number (%) 355 (47.6%) 0(0%)355 (100%) **WHO Category** 632 (84.8%) 346 (88.5%) 285 (80.7%) CMML-1 Number (%) CMML-2 Number (%) 113 (15.2%) 45 (11.5%) 68 (19.3%) Karyotype Normal Number (%) 500 (72.5%) 277 (75.7%) 223 (69.0%) Abnormal Number (%) 190 (27.5%) 89 (24.3%) 100 (31.0%) Spanish Cytogenetic Risk Category Number (%) 523 (75.8%) 292 (79.8%) 231 (71.5%) Low Intermediate Number (%) 118 (17.1%) 52 (14.2%) 65 (20.1%) High Number (%) 49 (7.1%) 22 (6.0%) 27 (8.4%) **GFM Risk Category** 40 (15.2%) Number (%) 247 (43.8%) 207 (68.8%) Intermediate Number (%) 202 (35.8%) 72 (23.9%) 130 (49.4%) Number (%) 115 (20.4%) 22 (7.3%) 93 (35.4%) High Mayo Molecular Risk Category Number (%) 51 (9.2%) 40 (13.4%) 11 (4.3%) Low 44 (17.2%) Intermediate-1 Number (%) 158 (28.5%) 114 (38.3%) Intermediate-2 Number (%) 165 (29.8%) 83 (27.9%) 82 (32.0%) High Number (%) 180 (32.5%) 61 (20.5%) 119 (46.5%) **CPSS-Molecular Risk Category** 70 (24.1%) 70 (13.0%) Number (%) 0 (0%) Intermediate-1 151 (28.1%) 117 (40.3%) 34 (13.8%) Number (%) Number (%) 47 (16.2%) Intermediate-2 117 (21.8%) 70 (28.3%) High Number (%) 199 (37.1%) 56 (19.3%) 143 (57.9%) **Mutation Statistics Number of Mutated Genes** 3 (0 - 8) 2 (0 - 8) 3(0-7)Median (range) **Mutation Profile** ASXL1 Number (%) 257 (45.3%) 113 (37.5%) 142 (54.0%) **BCOR** Number (%) 10 (1.8%) 4 (1.3%) 6 (2.3%) **BRAF** Number (%) 2 (0.4%) 2 (0.7%) 0 (0%) CALR Number (%) 2 (0.4%) 1 (0.3%) 1 (0.4%) CBL Number (%) 82 (14.5%) 37 (12.3%) 45 (17.1%) CEBPA Number (%) 17 (3.0%) 5 (1.7%) 12 (4.6%) CSF3R Number (%) 4 (0.7%) 0 (0%) 4 (1.5%) CUX1 Number (%) 2 (0.4%) 1 (0.3%) 1 (0.4%) DNMT3A Number (%) 27 (4.8%) 14 (4.7%) 13 (4.9%) 1 (0.3%) ETNK1 Number (%) 5 (0.9%) 4 (1.5%) 2 (0.7%) ETV6 Number (%) 5 (0.9%) 3 (1.1%) EZH2 Number (%) 25 (4.4%) 10 (3.3%) 15 (5.7%) FLT3 Number (%) 8 (1.4%) 2 (0.7%) 6 (2.3%) 1 (0.4%) GATA2 Number (%) 1 (0.2%) 0 (0%) 6 (2.0%) IDH1 Number (%) 9 (1.6%) 2 (0.8%) IDH2 Number (%) 36 (6.3%) 15 (5.0%) 21 (8.0%) JAK2 Number (%) 41 (7.2%) 10 (3.3%) 31 (11.8%) KIT Number (%) 23 (4.0%) 12 (4.0%) 10 (3.8%)

KRAS	Number (%)	53 (9.4%)	27 (9.0%)	26 (9.9%)
MPL	Number (%)	10 (1.8%)	4 (1.3%)	6 (2.3%)
NPM1	Number (%)	9 (1.6%)	6 (2.0%)	3 (1.1%)
NRAS	Number (%)	87 (15.3%)	33 (11.0%)	54 (20.5%)
PHF6	Number (%)	18 (3.2%)	14 (4.7%)	4 (1.5%)
PTPN11	Number (%)	18 (3.2%)	8 (2.7%)	10 (3.8%)
RAD21	Number (%)	4 (0.7%)	2 (0.7%)	2 (0.8%)
RUNX1	Number (%)	69 (12.2%)	43 (14.3%)	26 (9.9%)
SETBP1	Number (%)	36 (6.3%)	9 (3.0%)	27 (10.3%)
SF3B1	Number (%)	26 (4.6%)	20 (6.6%)	6 (2.3%)
SH2B3	Number (%)	7 (1.2%)	3 (1.0%)	4 (1.5%)
SRSF2	Number (%)	254 (44.8%)	144 (47.8%)	109 (41.4%)
STAG2	Number (%)	8 (1.4%)	4 (1.3%)	4 (1.5%)
SUZ12	Number (%)	0 (0%)	0 (0%)	0 (0%)
TET2	Number (%)	260 (45.9%)	156 (51.8%)	103 (39.2%)
TP53	Number (%)	21 (3.7%)	10 (3.3%)	11 (4.2%)
U2AF1	Number (%)	44 (7.8%)	23 (7.6%)	20 (7.6%)
WT1	Number (%)	3 (0.5%)	2 (0.7%)	1 (0.4%)
ZRSR2	Number (%)	26 (4.6%)	23 (7.6%)	3 (1.1%)
Mutation Groups				
RAS Pathway (BRAF, CBL, KRAS, NRAS, PTPN11)	Number (%)	215 (37.9%)	93 (30.9%)	122 (46.4%)
Outcomes				
Transformation to acute leukemia	Number (%)	158 (21.1%)	73 (18.7%)	84 (23.7%)
Death	Number (%)	529 (70.5%)	255 (65.2%)	270 (76.1%)