

# Routine clinical parameters and laboratory testing predict therapy-related myeloid neoplasms after treatment for breast cancer

Giulia Petrone,<sup>1\*</sup> Charles Gaulin,<sup>2\*</sup> Andriy Derkach,<sup>3</sup> Ashwin Kishtagari,<sup>4</sup> Mark E. Robson,<sup>5</sup> Rekha Parameswaran<sup>6#</sup> and Eytan M. Stein<sup>7#</sup>

<sup>1</sup>Department of Medicine, Mount Sinai Morningside and Mount Sinai West, New York, NY;

<sup>2</sup>Division of Hematology and Medical Oncology, Mayo Clinic, Phoenix, AZ; <sup>3</sup>Department of Biostatistics and Epidemiology, Memorial Sloan Kettering Cancer Center, New York, NY;

<sup>4</sup>Division of Hematology and Oncology, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN; <sup>5</sup>Breast Medicine Service, Memorial Sloan Kettering Cancer Center, New York, NY; <sup>6</sup>Division of Hematology, Memorial Sloan Kettering Cancer Center, New York, NY and <sup>7</sup>Leukemia Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA

<sup>o</sup>Current address: Division of Oncology, Washington University School of Medicine, St. Louis, MO, USA

\*GP and CG contributed equally as co-first authors.

#RP and EMS contributed equally as co-senior authors.

**Correspondence:** E. M. Stein  
[steine@mskcc.org](mailto:steine@mskcc.org)

**Received:** December 27, 2021.

**Accepted:** June 20, 2022.

**Prepublished:** June 30, 2022.

<https://doi.org/10.3324/haematol.2021.280437>

©2023 Ferrata Storti Foundation

Published under a CC BY-NC license



**Supplement - APPENDIX**

**Table 1S.** Basic description of all variables in the whole cohort.

<b>Variable</b>	<b>All patients</b>	<b>With t-MN (%)</b>	<b>Without t-MN (%)</b>	<b>p-value</b>
<b>t-MN</b> No Yes	99 107	NA NA	NA NA	NA NA
<b>WBC</b> 4-11 K/mcL <4 K/mcL >11 K/mcL	87 87 31	29 (33) 53 (61) 24 (77)	58 (67) 34 (39) 7 (23)	<0.0001
<b>ANC</b> <1.5 K/mcL ≥1.5 K/mcL	66 127	52 (79) 43 (34)	14 (21) 84 (66)	<0.0001
<b>Hgb</b> <12.2 g/dL ≥12.2 g/dL	163 42	94 (58) 12 (29)	69 (42) 30 (71)	0.0009
<b>MCV</b> 82-98 <82 >98	129 13 53	52 (40) 7 (54) 40 (75)	77 (60) 6 (46) 13 (25)	0.0001
<b>RDW</b> 11.5-14.5 >14.5	51 131	12 (24) 74 (56)	39 (76) 57 (44)	0.0001
<b>PLT</b>				0.0075

<100 K/mcL ≥100 K/mcL	98 105	60 (61) 44 (42)	38 (39) 61 (58)	
<b>Smear</b> Normal Abnormal	96 52	37 (39) 49 (94)	59 (61) 3 (6)	<0.0001
<b>Time from BC Dx to BMBx</b> >15 months <15 months	166 38	97 (58) 8 (21)	69 (42) 30 (79)	<0.0001
<b>Bone Mets</b> Absent Present	159 47	102 (64) 5 (11)	57 (36) 42 (89)	<0.0001
<b>Race</b> Asian Black White	8 36 152	3 (38) 15 (42) 83 (55)	5 (62) 21 (58) 69 (45)	0.273
<b>Treatment</b> Chemo and RT Chemo RT Surgery ± Hormone therapy	107 30 35 34	53 (50) 12 (40) 24 (69) 18 (53)	54 (50) 18 (60) 11 (31) 16 (47)	0.117

Online only

Legend: t-MN= therapy-related myeloid neoplasms; WBC= while blood cell; ANC=

absolute neutrophil count; Hgb= hemoglobin; MCV= mean corpuscular volume; RDW=

red cell distribution width; PLT= platelets; Normal smear= absence of blasts or dysplastic cells; Abnormal smear= presence of blasts or dysplastic cells; BC= breast cancer; Dx= diagnosis; BMBx= bone marrow biopsy; Mets= metastasis; chemo= chemotherapy; RT= radiotherapy; NA= not applicable. P-values are calculated using Fisher's exact test.

**Table 2S.** Type of chemotherapy received by the whole cohort.

<b>Therapy for breast cancer</b>	<b>Number of patients (%)</b>
Alkylating agent	121 (58.7)
Anthracycline/Topoisomerase II Inhibitors	102 (49.5)
Taxane	93 (45.1)
Topoisomerase I Inhibitors	2 (0.9)
Nucleotide analogs	56 (27.1)
Platinum	12 (5.8)
Vinca alkaloids	12 (5.8)

**Table 3S.** Stratification of treatment in the whole cohort.

	<b>All pts</b>	<b>With t-MN (%)</b>	<b>Without t-MN (%)</b>
<b>Chemo + RT ± Hormone therapy</b>	107	53 (50)	54 (50)
<b>Chemo ± Hormone therapy</b>	30	12 (40)	18 (60)
<b>RT ± Hormone therapy</b>	35	24 (69)	11 (31)
<b>Surgery ± Hormone therapy</b>	34	18 (53)	16 (47)

Online only

Legend: pts= patients; t-MN= therapy-related myeloid neoplasms; chemo= chemotherapy; RT= radiotherapy.

**Table 4S.** Distribution of cytogenetics grouped by treatment type in the cohort with t-MN.

	Total pts n= 107 (%)	Alkylating agents + Anthracycline ± RT and/or Platinum (50 pts)	Alkylating agents + Platinum and/or Nucleoside analog ± RT (9 pts)	Anthracycline only ± RT (2 pts)	Only RT (24 pts)	RT + Platinum + Taxane (3 pts)	No chemo or RT (17 pts)	Unknown regimen (2 pts)
Normal karyotype	33 (31)	10	3	2	6	1	10	1
del(7q)/ -7	14 (13)	8	3	-	-	2	-	1
del(5q)/ -5	23 (21.5)	10	3	-	6	1	2	1
inv(16)	2 (2)	2	-	-	-	-	-	-
t(8;16)	1 (1)	1	-	-	-	-	-	-
t(8;21)	7 (6.5)	6	-	-	1	-	-	-
Trisomy 8	14 (13)	4	1	-	7	1	1	-
Monosomy 18	6 (5.6)	3	-	-	1	1	1	-
t(11q23)/MLL mutation	10 (9)	8	1	-	1	-	-	-
Rearrangement 3q26	1 (1)	-	1	-	-	-	-	-
t(15;17)	2 (2)	1	-	-	-	-	1	-
Loss/mutation of p53	4 (3.7)	2	-	-	1	-	-	1
t(6;9)	3 (2.8)	2	1	-	-	-	-	-

Online only

Legend: t-MN= therapy-related myeloid neoplasms; pts= patients; RT= radiotherapy; chemo= chemotherapy.

**Table 5S.** Basic description of all variables in the cohort without bone metastasis.

<b>Variable</b>	<b>All patients</b>	<b>With t-MN (%)</b>	<b>Without t-MN (%)</b>	<b>p-value</b>
<b>t-MN</b> No Yes	57 102	NA NA	NA NA	NA NA
<b>WBC</b> <4 K/mcL >11 K/mcL 4-11 K/mcL	75 25 58	50 (67) 22 (88) 29 (50)	25 (33) 3 (12) 29 (50)	0.0029
<b>ANC</b> <1.5 K/mcL ≥1.5 K/mcL	62 85	50 (81) 40 (47)	12 (19) 45 (53)	<0.0001
<b>Hgb</b> <12.2 g/dL ≥12.2 g/dL	124 34	89 (72) 12 (35)	35 (28) 22 (65)	0.0002
<b>MCV</b> 82-98 <82 >98	97 10 43	50 (52) 7 (70) 37 (86)	47 (48) 3 (30) 6 (14)	0.0002
<b>RDW</b> 11.5-14.5 >14.5	45 92	12 (27) 69 (75)	33 (73) 23 (25)	<0.0001
<b>PLT</b> <100 K/mcL ≥100 K/mcL	71 85	58 (82) 41 (48)	13 (18) 44 (52)	<0.0001

<b>Smear</b> Normal Abnormal	69 47	35 (51) 47 (100)	34 (49) 0 (0)	<0.0001
<b>Time from BC Dx to BMBx</b> >15 months <15 months	129 28	92 (71) 8 (29)	37 (29) 20 (71)	<0.0001
<b>Race</b> Asian Black White	8 27 115	3 (38) 15 (56) 79 (69)	5 (62) 12 (44) 36 (31)	0.119
<b>Treatment</b> Chemo and RT Chemo RT Surgery ± Hormone therapy	80 23 29 27	51 (64) 11 (48) 22 (76) 18 (67)	29 (36) 12 (52) 7 (24) 9 (33)	0.223

Online only

Legend: t-MN= therapy-related myeloid neoplasms; WBC= white blood cell; ANC= absolute neutrophil count; Hgb= hemoglobin; MCV= mean corpuscular volume; RDW= red cell distribution width; PLT= platelets; Normal smear= absence of blasts or dysplastic cells; Abnormal smear= presence of blasts or dysplastic cells; BC= breast cancer; Dx= diagnosis; BMBx= bone marrow biopsy; chemo= chemotherapy; RT= radiotherapy; NA= not applicable. P-values are calculated using Fisher's exact test.

**Table 6S.** Basic description of all variables in the cohort with bone metastasis.

<b>Variable</b>	<b>Pts with bone mets n= 47</b>	<b>With t-MN n= 5 (%)</b>	<b>Without t-MN n= 42 (%)</b>	<b>p-value</b>
<b>t-MN</b> No Yes	42 5	NA NA	NA NA	NA NA
<b>WBC</b> <4 K/mcL >11 K/mcL 4-11 K/mcL	12 6 29	3 (25) 2 (33) 0 (0)	9 (75) 4 (67) 29 (100)	0.0059
<b>ANC</b> <1.5 K/mcL ≥1.5 K/mcL	4 42	2 (50) 3 (7)	2 (50) 39 (93)	0.053
<b>Hgb</b> <12.2 g/dL ≥12.2 g/dL	39 8	5 (13) 0 (0)	34 (87) 8 (100)	0.571
<b>MCV</b> 82-98 <82 >98	32 3 10	2 (6) 0 (0) 3 (30)	30 (94) 3 (100) 7 (70)	0.093
<b>RDW</b> 11.5-14.5 >14.5	6 39	0 (0) 5 (13)	6 (100) 34 (87)	1
<b>Time from BC Dx to BMBx</b> <15 months >15 months	10 37	2 (8) 3 (13)	22 (92) 20 (87)	0.666



<b>Race</b>				0.571
Black	9	4 (11)	33 (89)	
White	37	0 (0)	9 (100)	
<b>Treatment</b>				0.164
Chemo and RT	27	2 (7)	25 (93)	
Chemo	7	1 (14)	6 (86)	
RT	6	2 (33)	4 (67)	
Surgery ± Hormone therapy	7	0 (0)	7 (100)	

Online only

Legend: pts= patients; mets= metastasis; t-MN= therapy-related myeloid neoplasms;

WBC= while blood cell; ANC= absolute neutrophil count; Hgb= hemoglobin; MCV=

mean corpuscular volume; RDW= red cell distribution width; BC= breast cancer; Dx=

diagnosis; BMBx= bone marrow biopsy; chemo= chemotherapy; RT= radiotherapy; NA=

not applicable. P-values are calculated using Fisher's exact test.

**Table 7S.** Basic description of all variables in the cohort with negative peripheral smear.

<b>Variable</b>	<b>Pts with negative peripheral smear n= 96</b>	<b>With t-MN n= 37 (%)</b>	<b>Without t-MN n= 59 (%)</b>	<b>p-value</b>
<b>t-MN</b>				
No	59	NA	NA	

Yes	37	NA	NA	NA NA
<b>WBC</b> 4-11 K/mcL <4 K/mcL >11 K/mcL	44 41 10	9 (20) 22 (54) 5 (50)	35 (80) 19 (46) 5 (50)	0.0037
<b>ANC</b> <1.5 K/mcL ≥1.5 K/mcL	26 68	18 (69) 17 (25)	8 (31) 51 (75)	0.0001
<b>Hgb</b> <12.2 g/dL ≥12.2 g/dL	80 15	35 (44) 1 (7)	45 (56) 14 (93)	0.0076
<b>MCV</b> 82-98 <82 >98	64 7 21	19 (30) 2 (29) 13 (62)	45 (70) 5 (71) 8 (38)	0.028
<b>RDW</b> 11.5-14.5 >14.5	23 67	5 (22) 27 (40)	18 (78) 40 (60)	0.134
<b>Time from BC Dx to BMBx</b> <15 months >15 months	26 70	4 (15) 33 (47)	22 (85) 37 (53)	0.0002
<b>Bone Mets</b> Absent Present	69 27	4 (15) 33 (47)	22 (85) 37 (53)	0.004
<b>Race</b> Asian	4	1 (25)	3 (75)	0.093

Black	18	3 (17)	15 (83)	
White	71	30 (42)	41 (58)	
<b>Treatment</b>				0.316
Chemo and RT	48	15 (31)	33 (69)	
Chemo	14	5 (36)	9 (64)	
RT	20	11 (55)	9 (45)	
Surgery ± Hormone therapy	14	6 (43)	8 (57)	

Online only

Legend: pts= patients; mets= metastasis; t-MN= therapy-related myeloid neoplasms; WBC= while blood cell; ANC= absolute neutrophil count; Hgb= hemoglobin; MCV= mean corpuscular volume; RDW= red cell distribution width; BC= breast cancer; Dx= diagnosis; BMBx= bone marrow biopsy; chemo= chemotherapy; RT= radiotherapy; NA= not applicable. P-values are calculated using Fisher’s exact test.