SUPPLEMENTARY APPENDIX

Bone marrow megakaryocytic activation predicts fibrotic evolution of Philadelphia-negative myeloproliferative neoplasms

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Supplemental data

Table 1S

ET	Overall (n=23)
Age[1]	61.4 (42-75)
Male **Female**	9 (39.1%) 14 (60.9%)
JAK2-RT > 50%	7(30.4%)
CALR mut.	2 (8.7%)
CALR type 1 **CALR type 2**	1 (4.3%) 1 (4.3%)
MPL mut.	0 (0%)
Hgb[3]	14.3 (13.8-15.7)
LDH serum levels[4]	245.1 (180-322)
Palpable splenomegaly	4 (17.4%)
WBC[5]	9.8(7.1-11.8)
PLT[6]	615.3 (453-811)
A/V thrombosis	6 (26.1%)
Major bleeding	3 (13.0%)

[1]In years
[2]In months
[3](g/dL)
[4](UI/L)
[5](x 10^9 /L)
[6](x 10^9 /L)

Supplementary figure legend

Figure 1S

Kaplan-Meier curves for PFS of PV patients stratified for JAK2 status, bleeding and WBC count. Patients with JAK2 burden≥50% and history of bleeding (red line) had a significant correlation with a worse PFS (for JAK2 status, P=.0225, HR 2.1274, 95% CI from 1.1124 to 4.0683; for bleeding, P=.0174, HR 2.9615, 95% CI from 1.2104 to 7.2458) respect to those with JAK2 burden<50% and without history of bleeding (blu-line). Patients with WBC count≥11x10^9/l (red line) showed a certain trend toward significance with a worse PFS (P=.0823; HR 0.5171, 95% CI from 0.2458 to 1.0880) respect to those with WBC count<11x10^9/l (red line).

Figure 2S

Kaplan-Meier curves for early/prefibrotic PMF stratified for CALR mutations (type 1 and type 2 mutation), PLT count, WBC count, splenomegaly, LDH level and gender. Patients with WBC count≥11x10^9/l, CALR type 1 mutation, PLT≥450x10^9/l, palpable splenomegaly, LDH≥250UI/l and female gender (red line) had a significant correlation with a worse PFS (for WBC count, P<.0001, HR 1.9458, 95% CI from 1.4395 to 2.6303; for PLT count, P<.0001, HR 1.9993, 95% CI from 1.4597 to 2.7384; for splenomegaly, P<.0001, HR 1.8993, 95% CI from 1.4132 to 2.5524; for LDH level, P=.0025, HR 1.5678, 95% CI from 1.1710 to 2.0991; for gender, P=.0187, HR 1.4125, 95% CI from 1.0592 to 1.8835; for CALR status; CALR type 1 mutation versus CALR wild type, P<.0001, HR 2.1476, 95% CI from 1.4040 to 3.2850) respect to those with WBC count<11x10^9/l, CALR wild-type, PLT<450x10^9/l, absence of palpable splenomegaly, LDH<250UI/l and male gender (blu-line).

Figure 3S

Kaplan-Meier curves for PFS early/prefibrotic PMF and ET stratified for M-ACT parameter. ET patients that did not have a M-ACT in any case showed a significant correlation with a better PFS in comparison to both early/prefibrotic PMF with that without M-ACT (P<.0001).

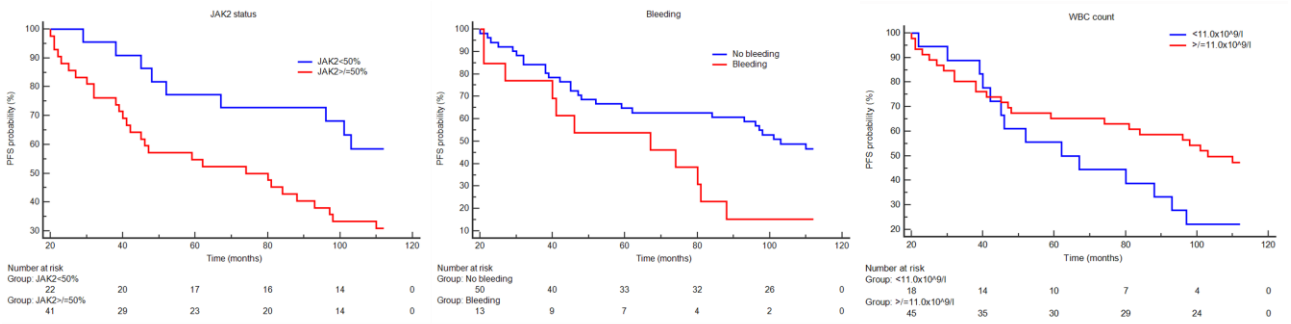

JAK2 status
PFS probability (%)
JAK2<50%
JAK2>/=50%
Time (months)
Number at risk
Group: JAK2<50%
22 20 17 16 14 0
Group: JAK2>/=50%
41 29 23 20 14 0
Bleeding
No bleeding
Bleeding
Time (months)
Number at risk
Group: No bleeding
50 40 33 32 26 0
Group: Bleeding
13 9 7 4 2 0
WBC count
<11.0x10^9/l
>/=11.0x10^9/l
Time (months)
Number at risk
Group: <11.0x10^9/l
18 14 10 7 4 0
Group: >/=11.0x10^9/l
45 35 30 29 24 0

Figure 1S

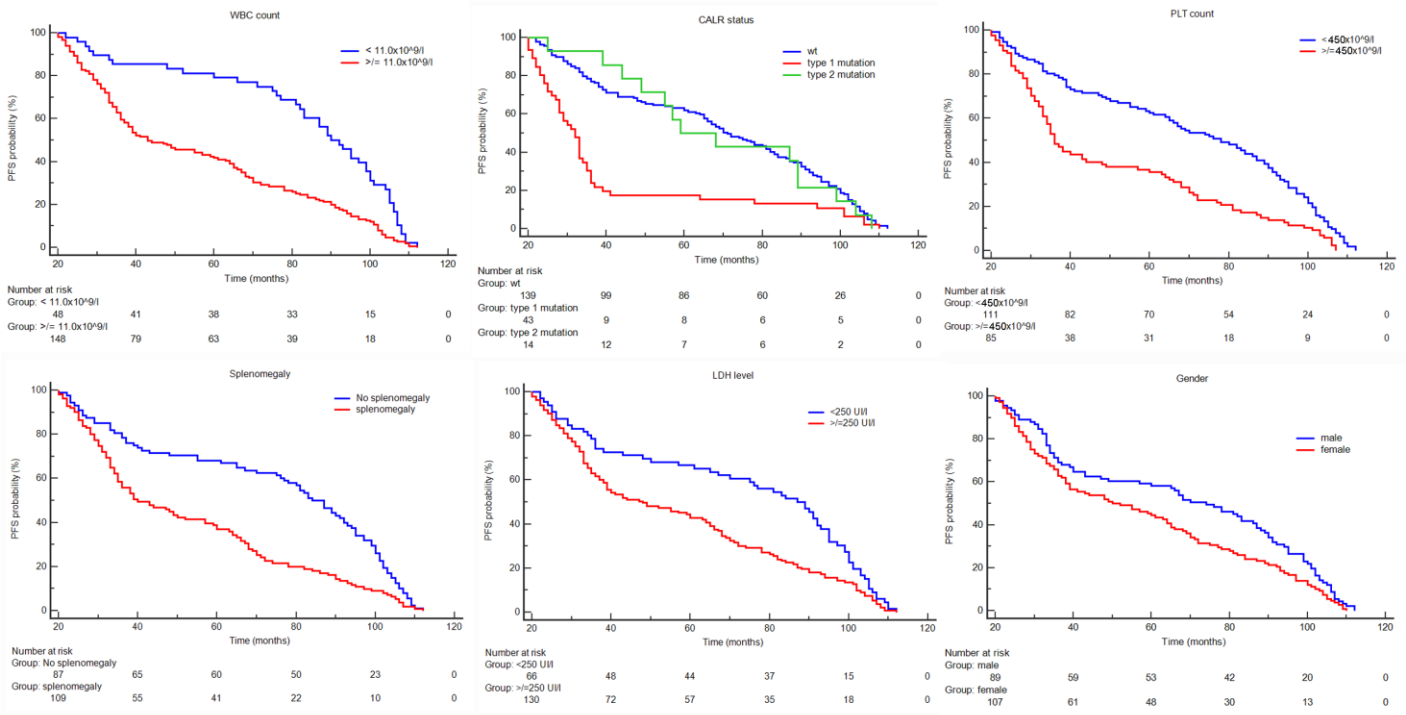
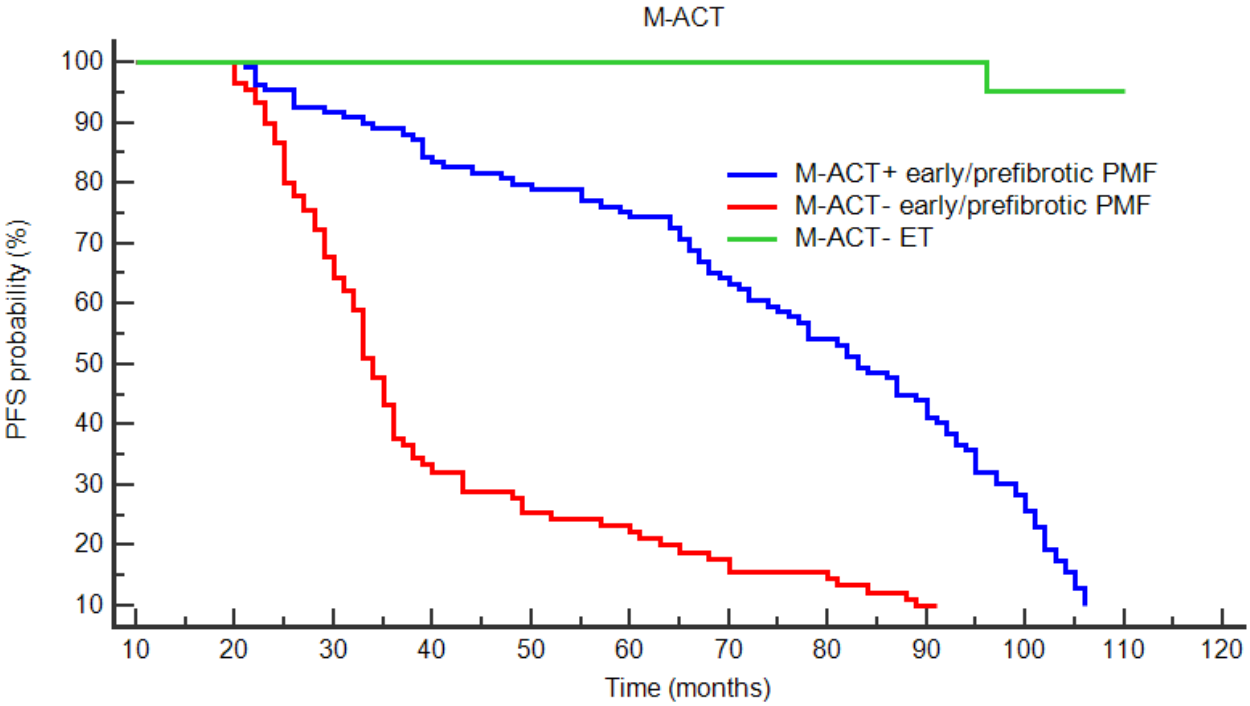

WBC count
PFS probability (%)
< 11.0x10^9/l
>/= 11.0x10^9/l
Time (months)
Number at risk
Group: < 11.0x10^9/l
48 41 38 33 15 0
Group: >/= 11.0x10^9/l
148 79 63 39 18 0
CALR status
wt
type 1 mutation
type 2 mutation
Number at risk
Group: wt
139 99 86 60 26 0
Group: type 1 mutation
43 9 8 6 5 0
Group: type 2 mutation
14 12 7 6 2 0
PLT count
<450x10^9/l
>/=450x10^9/l
Number at risk
Group: <450x10^9/l
111 82 70 54 24 0
Group: >/=450x10^9/l
85 38 31 18 9 0
Splenomegaly
No splenomegaly
splenomegaly
Number at risk
Group: No splenomegaly
87 65 60 50 23 0
Group: splenomegaly
109 55 41 22 10 0
LDH level
<250 UI/l
>/=250 UI/l
Number at risk
Group: <250 UI/l
66 48 44 37 15 0
Group: >/=250 UI/l
130 72 57 35 18 0
Gender
male
female
Number at risk
Group: male
89 59 53 42 20 0
Group: female
107 61 48 30 13 0

Figure 2S



Number at risk

Group: M-ACT+ early/prefibrotic PMF											
109	109	100	91	86	81	69	59	45	28	2	0
Group: M-ACT- early/prefibrotic PMF											
90	87	58	29	23	20	14	13	9	5	0	0
Group: M-ACT- ET											
23	23	23	23	23	23	23	22	21	20	0	0

Figure 3S