SUPPLEMENTAL DATA

Supplemental tables

Table S1: List of the 36 myeloid genes included in the Next Generation Sequencing (NGS) panel.

36 myeloid genes of NGS panel
JAK2
CALR
MPL
TET2
DNMT3A
ASXL1
EZH2
IDH1
IDH2
STEBP1
SRSF2
U2AF1
SF3B1
ZRSR2
ETNK1
CBL
KRAS
SH2B3
CSF3R
NRAS
KIT
BRAF
FLT3
HRAS
PTPN11
WT1
ABL1
NFE2
TP53
IKZF1
CEBPα
RUNX1
ETV6
CUX1
CCND2
NPM1

Table S2A: **PV patients' characteristics according to occurrence of arterial thrombotic events during follow-up.**

	All (n=362)	Patients with no arterial thrombotic event during FU (n=334)	Patients with arterial thrombotic events during FU (n=28)	p value
Age at MPN diagnosis (years), median (IQR)	51 [41;60]	50 [41;60]	54.5 [47;66]	**0.041**
Female nb (%)				0.532
No	190 (52.49%)	175 (52.40%)	15 (53.57%)	
Yes	172 (47.51%)	159 (47.60%)	13 (46.43%)	
WHO Performances status, nb (%)				0.643
0	100 (27.62%)	94 (28.14%)	6 (21.43%)	
1	23 (6.35%)	21 (6.29%)	2 (7.14%)	
2	0 (0%)	0 (0%)	0 (0%)	
3	0 (0%)	0 (0%)	0 (0%)	
4	0 (0%)	0 (0%)	0 (0%)	
Constitutional symptoms, nb (%)				0.460
No	146 (40.33%)	137 (41.02%)	9 (32.14%)	
Yes	9 (2.49%)	8 (2.40%)	1 (3.57%)	
Splenomegaly, nb (%)				0.268
No	104 (28.73%)	94 (28.14%)	10 (35.71%)	
Yes	85 (23.48%)	81 (24.25%)	4 (14.29%)	
Cardiovascular risk factors*, nb (%)				**0.004**
No	214 (59.12%)	205 (61.38%)	9 (32.14%)	
Yes	148 (40.88%)	129 (38.62%)	19 (67.86%)	
Hb (g/dL), median (IQR)	17.3 [15.8;19.1]	17.4 [15.6;19.2]	16.5 [16.2;17.4]	0.681
Ht (%), median (IQR)	52 [46.9;57.7]	52.35 [46.7;58]	50.7 [49;56]	0.196
Platelets (G/L), median (IQR)	478 [332;700]	468 [325;683]	656 [482;900]	**0.019**
WBC (G/L), median (IQR)	10 [7.8;13]	10 [7.81;13]	9.25 [7.15;13.8]	0.703
ANC (G/L), median (IQR)	6.6 [4.95;10.14]	6.69 [4.94;10.22]	5.4 [5.2;6.99]	0.605
Circulating Blasts, nb (%)				NA
No	276 (76.24%)	254 (76.05%)	22 (78.57%)	
≥ 1%	0 (0%)	0 (0%)	0 (0%)	
ELN-thrombosis score at diagnosis, nb (%)				0.167
Low	189 (52.22%)	178 (53.29%)	11 (39.29%)	
High	169 (46.69%)	152 (45.51%)	17 (60.71%)	
Thrombosis prior to or/and at diagnosis, nb (%)				0.663
No	260 (71.82%)	241 (72.16%)	19 (67.86%)	

Yes	102 (28.18%)	93 (27.84%)	9 (32.14%)	
Number of thrombotic event prior to or/and at diagnosis, median (IQR)	0 [0;1]	0 [0;1]	0 [0;1]	0.567
Arterial thrombosis prior to or/and at diagnosis, nb (%)				0.165
No	328 (90.61%)	305 (91.32%)	23 (82.14%)	
Yes	34 (9.39%)	29 (8.68%)	5 (17.86%)	
Venous thrombosis prior to or/and at diagnosis, nb (%)				0.622
No	292 (80.66%)	268 (80.24%)	24 (85.71%)	
Yes	70 (19.34%)	66 (19.76%)	4 (14.29%)	

**Cardiovascular risk factors include at least one of the following factors: smoking, arterial hypertension, diabetes or hypercholesterolemia.*

PV=Polycythemia Vera, IQR=Interquartile range, nb=Number of patients, Hb=Hemoglobin, Ht=Hematocrit, WBC=White blood cells, ANC=absolute neutrophil count, FU=Follow-up, IPSS=International Prognostic Scoring System, ELN=European Leukemia Net, IPSET= International Prognostic Score of Thrombosis for Essential Thrombocythemia.

Table S2B: PV patients' characteristics according to occurrence of venous thrombotic events during follow-up.

	All (n=362)	Patients with no venous thrombotic event during FU (n=328)	Patients with venous thrombotic events during FU (n=34)	p value
Age at MPN diagnosis (years), median (IQR)	51 [41;60]	50 [41;60]	52 [41;60]	0.644
Female nb (%)				0.368
No	190 (52.49%)	175 (53.35%)	15 (44.12%)	
Yes	172 (47.51%)	153 (46.65%)	19 (55.88%)	
WHO Performances status, nb (%)				0.062
0	100 (27.62%)	95 (28.96%)	5 (14.71%)	
1	23 (6.35%)	19 (5.79%)	4 (11.76%)	
2	0 (0%)	0 (0%)	0 (0%)	
3	0 (0%)	0 (0%)	0 (0%)	
4	0 (0%)	0 (0%)	0 (0%)	
Constitutional symptoms, nb (%)				0.146
No	146 (40.33%)	136 (41.46%)	10 (29.41%)	
Yes	9 (2.49%)	7 (2.13%)	2 (5.88%)	
Splenomegaly, nb (%)				0.611
No	104 (28.73%)	96 (29.27%)	8 (23.53%)	
Yes	85 (23.48%)	76 (23.17%)	9 (26.47%)	
Cardiovascular risk factors*, nb (%)				0.098
No	214 (59.12%)	189 (57.62%)	25 (73.53%)	
Yes	148 (40.88%)	139 (42.38%)	9 (26.47%)	
Hb (g/dL), median (IQR)	17.3 [15.8;19.1]	17.3 [15.8;19]	17.9 [15.65;19.55]	0.700
Ht (%), median (IQR)	52 [46.9;57.7]	51.95 [46.95;57.1]	53.3 [46.2;62]	0.540
Platelets (G/L), median (IQR)	478 [332;700]	491 [332;700]	414 [343;606]	0.391
WBC (G/L), median (IQR)	10 [7.8;13]	10 [7.8;13]	8.99 [7.85;11.2]	0.300
ANC (G/L), median (IQR)	6.6 [4.95;10.14]	6.69 [4.95;10.3]	6.06 [3.7;8.33]	0.602
Circulating Blasts, nb (%)				NA
No	276 (76.24%)	248 (75.61%)	28 (82.35%)	
≥ 1%	0 (0%)	0 (0%)	0 (0%)	
ELN-thrombosis score at diagnosis, nb (%)				1
Low	189 (52.22%)	171 (52.13%)	18 (52.94%)	
High	169 (46.69%)	153 (46.65%)	16 (47.06%)	
Thrombosis prior to or/and at diagnosis, nb (%)				1
No	260 (71.82%)	235 (71.65%)	25 (73.53%)	

Yes	102 (28.18%)	93 (28.35%)	9 (26.47%)	
Number of thrombotic event prior to or/and at diagnosis, median (IQR)	0 [0;1]	0 [0;1]	0 [0;1]	0.258
Arterial thrombosis prior to or/and at diagnosis, nb (%)				1
No	328 (90.61%)	297 (90.55%)	31 (91.18%)	
Yes	34 (9.39%)	31 (9.45%)	3 (8.82%)	
Venous thrombosis prior to or/and at diagnosis, nb (%)				1
No	292 (80.66%)	264 (80.49%)	28 (82.35%)	
Yes	70 (19.34%)	64 (19.51%)	6 (17.65%)	

**Cardiovascular risk factors include at least one of the following factors: smoking, arterial hypertension, diabetes or hypercholesterolemia.*

PV=Polycythemia Vera, IQR=Interquartile range, nb=Number of patients, Hb=Hemoglobin, Ht=Hematocrit, WBC=White blood cells, ANC=absolute neutrophil count, FU=Follow-up, IPSS=International Prognostic Scoring System, ELN=European Leukemia Net, IPSET= International Prognostic Score of Thrombosis for Essential Thrombocythemia.

Table S3A: **ET patients' characteristics according to occurrence of arterial thrombotic events during follow-up.**

	All (n=494)	Patients with no arterial thrombotic event during FU (n=456)	Patients with arterial thrombotic event during FU (n=38)	p value
Age at MPN diagnosis (years), median (IQR)	47 [37;58]	47 [37;58]	54 [41;64]	**0.050**
Female nb (%)				0.293
No	170 (34.41%)	154 (33.77%)	16 (42.11%)	
Yes	324 (65.59%)	302 (66.23%)	22 (57.89%)	
WHO Performances status, nb (%)				0.648
0	159 (32.19%)	151 (33.11%)	8 (21.05%)	
1	25 (5.06%)	23 (5.04%)	2 (5.26%)	
2	0 (0%)	0 (0%)	0 (0%)	
3	1 (0.20%)	1 (0.22%)	0 (0%)	
4	0 (0%)	0 (0%)	0 (0%)	
Constitutional symptoms, nb (%)				1
No	208 (42.11%)	198 (43.42%)	10 (26.32%)	
Yes	9 (1.82%)	9 (1.97%)	0 (0%)	
Splenomegaly, nb (%)				0.697
No	210 (42.51%)	199 (43.64%)	11 (28.95%)	
Yes	40 (8.10%)	39 (8.55%)	1 (2.63%)	
Cardiovascular risk factors*, nb (%)				**<0.0001**
No	299 (60.53%)	289 (63.38%)	10 (26.32%)	
Yes	195 (39.47%)	167 (36.62%)	28 (73.68%)	
Hb (g/dL), median (IQR)	13.6 [12.8;14.5]	13.6 [12.8;14.5]	13.8 [12.3;14.4]	0.150
Ht (%), median (IQR)	41.2 [39;44.7]	41.1 [39;44.7]	42 [38.8;42]	0.939
Platelets (G/L), median (IQR)	733 [581;1000]	724 [581;992]	898 [600;1400]	0.160
WBC (G/L), median (IQR)	8.41 [6.78;10.66]	8.46 [6.78;10.8]	7.32 [6.1;8.9]	0.163
ANC (G/L), median (IQR)	5.67 [4.42;7.14]	5.7 [4.5;7.16]	4.97 [3.48;6.82]	0.386
Circulating Blasts, nb (%)				NA
No	398 (80.57%)	366 (80.26%)	32 (84.21%)	
≥ 1%	96 (19.43%)	0 (0%)	0 (0%)	
ELN-thrombosis score at diagnosis, nb (%)				**0.033**
Low	317 (64.17%)	299 (65.57%)	18 (47.37%)	
High	174 (35.22%)	154 (33.77%)	20 (52.63%)	
IPSET-thrombosis score at diagnosis, nb (%)				0.218

Low	185 (37.45%)	175 (38.37%)	10 (26.32%)	
Intermediate	122 (24.70%)	113 (24.78%)	9 (23.68%)	
High	184 (37.25%)	165 (36.18%)	19 (50%)	
Thrombosis prior to or/and at diagnosis, nb (%)				0.676
No	392 (79.35%)	363 (79.61%)	29 (76.32%)	
Yes	102 (20.65%)	93 (20.39%)	9 (23.68%)	
Number of thrombotic event prior to or/and at diagnosis, median (IQR)	0 [0;0]	0 [0;0]	0 [0;0]	0.980
Arterial thrombosis prior to or/and at diagnosis, nb (%)				0.070
No	436 (88.26%)	406 (89.04%)	30 (78.95%)	
Yes	58 (11.74%)	50 (10.96%)	8 (21.05%)	
Venous thrombosis prior to or/and at diagnosis, nb (%)				0.158
No	445 (90.08%)	408 (89.47%)	37 (97.37%)	
Yes	49 (9.92%)	48 (10.53%)	1 (2.63%)	

**Cardiovascular risk factors include at least one of the following factors: smoking, arterial hypertension, diabetes or hypercholesterolemia.*

ET=Essential Thrombocytopenia, IQR=Interquartile range, nb=Number of patients, Hb=Hemoglobin, Ht=Hematocrit, WBC=White blood cells, ANC=absolute neutrophil count, FU=Follow-up, IPSS=International Prognostic Scoring System, ELN=European Leukemia Net, IPSET=International Prognostic Score of Thrombosis for Essential Thrombocythemia.

Table S3B: **ET patients' characteristics according to occurrence of venous thrombotic events during follow-up.**

	All (n=494)	Patients with no venous thrombotic event during FU (n=463)	Patients with venous thrombotic event during FU (n=31)	p value
Age at MPN diagnosis (years), median (IQR)	47 [37;58]	48 [37;58.5]	39 [25;53]	0.014
Female nb (%)				0.848
No	170 (34.41%)	160 (3456%)	10 (32.26%)	
Yes	324 (65.59%)	303 (65.44%)	21 (67.74%)	
WHO Performances status, nb (%)				1
0	159 (32.19%)	153 (33.05%)	6 (19.35%)	
1	25 (5.06%)	24 (5.18%)	1 (3.23%)	
2	0 (0%)	1 (0.22%)	0 (0%)	
3	1 (0.20%)	0 (0%)	0 (0%)	
4	0 (0%)	0 (0%)	0 (0%)	
Constitutional symptoms, nb (%)				1
No	208 (42.11%)	198 (42.76%)	10 (32.26%)	
Yes	9 (1.82%)	9 (1.94%)	0 (0%)	
Splenomegaly, nb (%)				0.221
No	210 (42.51%)	199 (42.98%)	11 (35.48%)	
Yes	40 (8.10%)	40 (8.64%)	20 (64.52%)	
Cardiovascular risk factors*, nb (%)				0.57
No	299 (60.53%)	282 (60.91%)	17 (54.84%)	
Yes	195 (39.47%)	181 (39.09%)	14 (45.16%)	
Hb (g/dL), median (IQR)	13.6 [12.8;14.5]	13.6 [12.8;14.5]	13 [13.85;14.9]	0.339
Ht (%), median (IQR)	41.2 [39;44.7]	41.1 [38.9;44.5]	44.2 [39.8;44.8]	0.325
Platelets (G/L), median (IQR)	733 [581;1000]	745 [586;1000]	600 [533;899]	0.106
WBC (G/L), median (IQR)	8.41 [6.78;10.66]	8.41 [6.76;10.77]	8.55 [7.68;10.5]	0.977
ANC (G/L), median (IQR)	5.67 [4.42;7.14]	5.69 [4.42; 7.15]	4.95 [4.85;5.8]	0.49
Circulating Blasts, nb (%)				NA
No	398 (80.57%)	371 (80.13%)	27 (87.10%)	
≥ 1%	96 (19.43%)	0 (0%)	0 (0%)	
ELN-thrombosis score at diagnosis, nb (%)				0.252
Low	317 (64.17%)	300 (64.80%)	17 (54.84%)	
High	174 (35.22%)	160 (34.58%)	14 (45.16%)	
IPSET-thrombosis score at diagnosis, nb (%)				0.053
Low	185 (37.44%)	178 (38.44%)	7 (22.58%)	
Intermediate	122 (24.70%)	116 (25.05%)	6 (19.35%)	

High	184 (37.25%)	166 (35.85%)	18 (58.06%)	
Thrombosis prior to or/and at diagnosis, nb (%)				0.063
No	392 (79.35%)	372 (80.35%)	20 (64.52%)	
Yes	102 (20.65%)	91 (19.65%)	11 (35.48%)	
Number of thrombotic event prior to or/and at diagnosis, median (IQR)	0 [0;0]	0 [0;0]	0 [0;0]	**0.045**
Arterial thrombosis prior to or/and at diagnosis, nb (%)				1
No	436 (88.26%)	408 (88.12%)	28 (90.32%)	
Yes	58 (11.74%)	55 (11.88%)	3 (9.68%)	
Venous thrombosis prior to or/and at diagnosis, nb (%)				**0.007**
No	445 (90.08%)	422 (91.14%)	23 (74.19%)	
Yes	49 (9.92%)	41 (8.86%)	8 (25.81%)	

**Cardiovascular risk factors include at least one of the following factors: smoking, arterial hypertension, diabetes or hypercholesterolemia.*

ET=Essential Thrombocytopenia, IQR=Interquartile range, nb=Number of patients, Hb=Hemoglobin, Ht=Hematocrit, WBC=White blood cells, ANC=absolute neutrophil count, FU=Follow-up, IPSS=International Prognostic Scoring System, ELN=European Leukemia Net, IPSET=International Prognostic Score of Thrombosis for Essential Thrombocythemia.

Table S4A: **MF patients' characteristics according to occurrence of arterial thrombotic events during follow-up.**

	All (n=161)	Patients with no arterial thrombotic event during FU (n=158)	Patients with arterial thrombotic events during FU (n=3)	p value
Age at MPN diagnosis (years), median (IQR)	58 [49;65]	58 [48;65]	61 [59;66]	0.385
Female nb (%)				0.553
No	111 (68.94%)	108 (68.35%)	3 (100%)	
Yes	50 (31.06%)	50 (31.65%)	0 (0%)	
WHO Performances status, nb (%)				0.588
0	32 (19.88)	30 (18.99%)	2 (66.67%)	
1	53 (32.92%)	52 (32.91%)	1 (33.33%)	
2	17 (10.56%)	17 (10.76%)	0 (0%)	
3	1 (0.62%)	1 (0.63%)	0 (0%)	
4	0 (0%)	0 (0%)	0 (0%)	
Constitutional symptoms, nb (%)				0.277
No	69 (42.86%)	66 (41.77%)	3 (100%)	
Yes	45 (27.95%)	45 (28.48%)	0 (0%)	
Splenomegaly, nb (%)				1
No	26 (16.15%)	26 (16.46%)	2 (66.67%)	
Yes	117 (72.67%)	115 (72.78%)	1 (33.33%)	
Cardiovascular risk factors*, nb (%)				0.587
No	89 (55.28%)	88 (55.70%)	1 (33.33%)	
Yes	72 (44.72%)	70 (44.30%)	2 (66.67%)	
Hb (g/dL), median (IQR)	11.25 [9.5;13.1]	11.2 [9.5;13.1]	12.55 [11.5;13.6]	0.391
Ht (%), median (IQR)	35.7 [30.2;39.8]	35.7 [30.1;39.8]	36.7 [33.3;40.1]	0.706
Platelets (G/L), median (IQR)	240 [132;510]	238 [132;500]	774 [535;1012]	0.078
WBC (G/L), median (IQR)	11.1 [7.1;16]	11.1 [7.1;16]	12.85 [10.3;15.4]	0.675
ANC (G/L), median (IQR)	8.17 [4.25;11.9]	8.17 [4.11;12]	7.8 [5.9;9.7]	0.837
Circulating Blasts, nb (%)				1
No	64 (39.75%)	62 (39.24%)	2 (66.67%)	
≥ 1%	43 (26.71%)	42 (26.58%)	1 (33.33%)	
IPSS score, nb (%)				1
Low	27 (16.77%)	26 (16.46%)	1 (33.33%)	
Intermediate 1	24 (14.91%)	24 (15.19%)	0 (0%)	
Intermediate 2	29 (18.01%)	28 (17.72%)	1 (33.33%)	
High	20 (12.42%)	20 (12.65%)	0 (0%)	
Thrombosis prior to or/and at diagnosis, nb (%)				**0.004**
No	135 (83.85%)	135 (85.44%)	0 (0%)	

Yes	26 (16.15%)	23 (14.56%)	3 (100%)	
Number of thrombotic event prior to or/and at diagnosis, median (IQR)	0 [0;0]	0 [0;0]	1 [1;1]	**0.0001**
Arterial thrombosis prior to or/and at diagnosis, nb (%)				**0.030**
No	144 (89.44%)	143 (90.51%)	1 (33.33%)	
Yes	17 (10.56%)	15 (9.49%)	2 (66.67%)	
Venous thrombosis prior to or/and at diagnosis, nb (%)				0.192
No	150 (93.17%)	148 (93.67%)	2 (66.67%)	
Yes	11 (6.83%)	10 (6.33%)	1 (33.33%)	

**Cardiovascular risk factors include at least one of the following factors: smoking, arterial hypertension, diabetes or hypercholesterolemia.*

MF=Myelofibrosis, IQR=Interquartile range, nb=Number of patients, Hb=Hemoglobin, Ht=Hematocrit, WBC=White blood cells, ANC=absolute neutrophil count, FU=Follow-up, IPSS=International Prognostic Scoring System, IPSS=International Prognosis Scoring System.

Table S4B: **MF patients' characteristics according to occurrence of venous thrombotic events during follow-up.**

	All (n=161)	Patients with no venous thrombotic event during FU (n=151)	Patients with venous thrombotic events during FU (n=10)	p value
Age at MPN diagnosis (years), median (IQR)	58 [49;65]	58 [48;65]	59.5 [49;67]	0.953
Female nb (%)				0.725
No	111 (68.94%)	103 (68.21%)	8 (80%)	
Yes	50 (31.06%)	48 (31.79%)	2 (20%)	
WHO Performances status, nb (%)				0.776
0	32 (19.88)	30 (19.87%)	2 (20%)	
1	53 (32.92%)	50 (33.11%)	3 (30%)	
2	17 (10.56%)	15 (9.93%)	2 (20%)	
3	1 (0.62%)	1 (0.66%)	0 (0%)	
4	0 (0%)	0 (0%)	0 (0%)	
Constitutional symptoms, nb (%)				0.476
No	69 (42.86%)	63 (41.72%)	6 (60%)	
Yes	45 (27.95%)	43 (28.48%)	2 (20%)	
Splenomegaly, nb (%)				0.667
No	26 (16.15%)	24 (15.89%)	2 (20%)	
Yes	117 (72.67%)	110 (72.85%)	7 (70%)	
Cardiovascular risk factors*, nb (%)				0.054
No	89 (55.28%)	87 (57.62%)	2 (20%)	
Yes	72 (44.72%)	64 (42.38%)	8 (80%)	
Hb (g/dL), median (IQR)	11.25 [9.5;13.1]	11.2 [9.5;13]	12.95 [9.6;14.95]	0.222
Ht (%), median (IQR)	35.7 [30.2;39.8]	35.7 [30.2;39.7]	34.85 [30.4;43.7]	0.663
Platelets (G/L), median (IQR)	240 [132;510]	235 [121;510]	282 [194;338]	0.438
WBC (G/L), median (IQR)	11.1 [7.1;16]	11.06 [6.8;16]	14.07 [8.8;18.51]	0.451
ANC (G/L), median (IQR)	8.17 [4.25;11.9]	7.6 [4.11;11.8]	9.5 [5.39;12.97]	0.459
Circulating Blasts, nb (%)				0.14
No	64 (39.75%)	57 (37.75%)	7 (70%)	
≥ 1%	43 (26.71%)	42 (27.81%)	1 (10%)	
IPSS score, nb (%)				0.144
Low	27 (16.77%)	24 (15.89%)	3 (30%)	
Intermediate 1	24 (14.91%)	24 (15.89%)	0 (0%)	
Intermediate 2	29 (18.01%)	28 (18.54%)	1 (10%)	
High	20 (12.42%)	19 (12.58%)	1 (10%)	
Thrombosis prior to or/and at diagnosis, nb (%)				0.057
No	135 (83.85%)	129 (85.43%)	6 (60%)	

Yes	26 (16.15%)	22 (14.57%)	4 (40%)	
Number of thrombotic event prior to or/and at diagnosis, median (IQR)	0 [0;0]	0 [0;0]	0 [0;1]	**0.021**
Arterial thrombosis prior to or/and at diagnosis, nb (%)				0.074
No	144 (89.44%)	137 (90.73%)	7 (70%)	
Yes	17 (10.56%)	14 (9.27%)	3 (30%)	
Venous thrombosis prior to or/and at diagnosis, nb (%)				0.141
No	150 (93.17%)	142 (94.04%)	8 (80%)	
Yes	11 (6.83%)	9 (5.96%)	2 (20%)	

**Cardiovascular risk factors include at least one of the following factors: smoking, arterial hypertension, diabetes or hypercholesterolemia.*

MF=Myelofibrosis, IQR=Interquartile range, nb=Number of patients, Hb=Hemoglobin, Ht=Hematocrit, WBC=White blood cells, ANC=absolute neutrophil count, FU=Follow-up, IPSS=International Prognostic Scoring System, IPSS=International Prognosis Scoring System.

Table S5A: Type of arterial and venous thrombosis associated to MPN.

	Thrombosis prior to and/or at diagnosis (n=292 events)	Thrombosis during FU (n=172 events)
Arterial thrombotic events, nb of events (%)	**130 (44.52%)**	**75 (43.60%)**
Type of arterial thrombosis		
AMI	42 (32.30%)	24 (32%)
Stroke	45 (34.61%)	20 (26.67%)
TIA	27 (20.76%)	18 (24%)
Peripheral arterial ischemia	15 (11.53%)	13 (17.33%)
Other	1 (0.769%)	0 (0%)
Venous thrombotic events, nb of events (%)	**162 (55.48%)**	**97 (56.40%)**
Type of venous thrombosis		
Pulmonary embolism	11 (6.79%)	13 (13.40%)
Superficial vein thrombosis	11 (6.79%)	13 (13.40%)
Deep vein thrombosis	38 (23.45%)	27 (27.83%)
Cerebral thrombosis	9 (5.56%)	8 (8.24%)
Splanchnic thrombosis	93 (57.40%)	36 (37.11%)

MPN=Myeloproliferative Neoplasms, FU=Follow-up, nb=number, AMI=Acute Myocardial Infarction, TIA=Transient Ischemic Attack.

Table S5B: Type of arterial and venous thrombosis associated to PV.

	Thrombosis prior to and/or at diagnosis (n=114 events)	Thrombosis during FU (n=69 events)
Arterial thrombotic events, nb of events (%)	**37 (32.45%)**	**29 (42.03%)**
Type of arterial thrombosis		
AMI	8 (21.62%)	12 (41.37%)
Stroke	18 (48.64%)	6 (20.68%)
TIA	8 (21.62%)	6 (20.68%)
Peripheral arterial ischemia	2 (5.405%)	5 (17.24%)
Other	1 (2.702%)	0 (0%)
Venous thrombotic events, nb of events (%)	**77 (67.54%)**	**40 (57.97%)**
Type of venous thrombosis		
Pulmonary embolism	4 (5.194%)	4 (10%)
Superficial vein thrombosis	2 (2.597%)	9 (22.5%)
Deep vein thrombosis	19 (24.67%)	15 (37.5%)
Cerebral thrombosis	1 (1.298%)	1 (2.5%)
Splanchnic thrombosis	51 (66.23%)	11 (27.5%)

PV=Polycythemia Vera, FU=Follow-up, nb=number, AMI=Acute Myocardial Infarction, TIA=Transient Ischemic Attack.

Table S5C: Type of arterial and venous thrombosis associated to ET.

	Thrombosis prior to and/or at diagnosis (n=122 events)	Thrombosis during FU (n=80 events)
Arterial thrombotic events, nb of events (%)	**67 (54.92%)**	**39 (48.75%)**
Type of arterial thrombosis		
AMI	21 (31.34%)	8 (20.51%)
Stroke	25 (37.31%)	12 (30.76%)
TIA	13 (19.40%)	11 (28.20%)
Peripheral arterial ischemia	8 (11.94%)	8 (20.51%)
Other	0 (0%)	0 (0%)
Venous thrombotic events, nb of events (%)	**55 (45.08%)**	**41 (51.25%)**
Type of venous thrombosis		
Pulmonary embolism	3 (5.45%)	4 (9.75%)
Superficial vein thrombosis	8 (14.54%)	4 (9.75%)
Deep vein thrombosis	16 (29.09%)	12 (29.26%)
Cerebral thrombosis	5 (9.09%)	4 (9.75%)
Splanchnic thrombosis	23 (41.81%)	17 (41.46%)

ET=Essential Thrombocytopenia, FU=Follow-up, nb=number, AMI=Acute Myocardial Infarction, TIA=Transient Ischemic Attack.

Table S5D: Type of arterial and venous thrombosis associated to MF.

	Thrombosis prior to and/or at diagnosis (n=30 events)	Thrombosis during FU (n= 14 events)
Arterial thrombotic events, nb of events (%)	**19 (63.33%)**	**3 (21.42%)**
Type of arterial thrombosis		
AMI	9 (47.36%)	2 (66.67%)
Stroke	1 (5.26%)	0 (0%)
TIA	6 (31.57%)	1 (33.33%)
Peripheral arterial ischemia	3 (15.79%)	0 (0%)
Other	0 (0%)	0 (0%)
Venous thrombotic events, nb of events (%)	**11 (36.67%)**	**11 (78.57%)**
Type of venous thrombosis		
Pulmonary embolism	3 (27.27%)	4 (36.36%)
Superficial vein thrombosis	1 (9.090%)	0 (0%)
Deep vein thrombosis	0 (0%)	0 (0%)
Cerebral thrombosis	3 (27.27%)	0 (0%)
Splanchnic thrombosis	4 (36.36%)	7 (63.64%)

MF=Myelofibrosis, FU=Follow-up, nb=number, AMI=Acute Myocardial Infarction, TIA=Transient Ischemic Attack.

Table S6A: MPN patients' cytogenetic and molecular characteristics according to occurrence of arterial thrombotic events during follow-up.

	All (n=1055)	Patients with no arterial thrombotic event during FU (n=983)	Patients with arterial thrombotic events during FU (n=72)	p value
Karyotype, nb (%)				0.899
Normal	99 (9.38%)	91 (9.26%)	8 (11.11%)	
Not normal excluding complex/monosomal	57 (5.40%)	52 (5.29%)	5 (6.94%)	
Complex/monosomal	9 (0.85%)	8 (0.81%)	1 (1.39%)	
***JAK2 V617F* mutation, nb (%)**				0.493
No	320 (30.33%)	299 (30.42%)	21 (29.17%)	
Yes	735 (69.67%)	684 (69.58%)	51 (70.83%)	
***JAK2* exon 12 mutation, nb (%)**				1
No	1048 (99.34%)	976 (99.29%)	72 (100%)	
Yes	7 (0.66%)	7 (0.71%)	0 (0%)	
***CALR* exon 9 mutation, nb (%)**				0.325
No	880 (83.41%)	823 (83.72%)	57 (79.17%)	
Yes	175 (16.59%)	160 (16.28%)	15 (20.83%)	
***MPL* exon 10 mutation, nb (%)**				0.755
No	1014 (96.11%)	945 (96.13%)	69 (95.83%)	
Yes	41 (3.89%)	38 (3.87%)	3 (4.17%)	
Triple negative, nb (%)				0.143
No	958 (90.81%)	889 (90.44%)	69 (95.83%)	
Yes	97 (9.19%)	94 (9.56%)	3 5(4.17%)	
Number of additional mutations, median (IQR)	1 [0;2]	1 [0;2]	1 [0;2.5]	0.065
***TET2* mutation**				**0.040**
No	814 (77.16%)	766 (77.92%)	48 (66.67%)	
Yes	241 (22.84%)	217 (22.08%)	24 (33.33%)	
***ASXL1* mutation**				0.104
No	878 (83.22%)	813 (82.71%)	65 (90.28%)	
Yes	177 (16.78%)	170 (17.29%)	7 (9.72%)	
***DNMT3A* mutation**				**0.011**
No	862 (81.71%)	812 (82.60%)	50 (69.44%)	
Yes	193 (18.29%)	171 (17.40%)	22 (30.56%)	
***EZH2* mutation**				0.571
No	1006 (95.36%)	938 (95.42%)	68 (94.44%)	
Yes	49 (4.64%)	45 (4.58%)	4 (5.56%)	
***IDH1* mutation**				1
No	1044 (98.96%)	972 (98.88%)	72 (100%)	

Yes	11 (1.04%)	11 (1.12%)	0 (0%)	
***IDH2* mutation**				1
No	1032 (97.82%)	961 (97.76%)	71 (98.61%)	
Yes	23 (2.18%)	22 (2.24%)	1 (1.39%)	
***SETBP1* mutation**				1
No	1048 (96.78%)	976 (99.29%)	72 (100%)	
Yes	7 (0.66%)	7 (0.71%)	0 (0%)	
***SRSF2* mutation**				0.408
No	1030 (97.63%)	958 (97.46%)	72 (100%)	
Yes	25 (2.37%)	25 (2.54%)	0 (0%)	
***U2AF1* mutation**				0.163
No	1021 (96.78%)	949 (96.54%)	72 (100%)	
Yes	34 (3.22%)	34 (3.46%)	0 (0%)	
***SF3B1* mutation**				0.106
No	1014 (96.11%)	942 (95.83%)	72 (100%)	
Yes	41 (3.89%)	41 (4.17%)	0 (0%)	
***ZRSR2* mutation**				1
No	1040 (98.58%)	969 (98.58%)	71 (98.61%)	
Yes	15 (1.42%)	14 (1.42%)	1 (1.39%)	
***NFE2* mutation**				0.092
No	1000 (94.79%)	935 (95.12%)	65 (90.28%)	
Yes	55 (5.21%)	48 (4.88%)	7 (9.72%)	
***TP53* mutation**				0.789
No	999 (94.69%)	931 (94.71%)	68 (94.44%)	
Yes	56 (5.31%)	52 (5.29%)	4 (5.56%)	
***IKZF1* mutation**				1
No	1054 (99.91%)	982 (99.90%)	72 (100%)	
Yes	1 (0.09%)	1 (0.10%)	0 (0%)	
***CEBPα* mutation**				0.132
No	1053 (99.81%)	982 (99.90%)	71 (98.61%)	
Yes	2 (0.19%)	1 (0.10%)	1 (1.39%)	
***CUX1* mutation**				0.24
No	1030 (97.63%)	961 (97.76%)	69 (95.83%)	
Yes	25 (2.37%)	22 (2.24%)	3 (4.17%)	
***RUNX1* mutation**				1
No	1043 (98.86%)	971 (98.78%)	72 (100%)	
Yes	12 (1.14%)	12 (1.22%)	0 (0%)	
***ETV6* mutation**				1
No	1046 (99.15%)	974 (99.08%)	72 (100%)	
Yes	9 (0.85%)	9 (0.92%)	0 (0%)	
***CBL* mutation**				0.167
No	1002 (94.98%)	936 (95.22%)	66 (91.67%)	

Yes	53 (5.02%)	47 (4.78%)	6 (8.33%)	
***KRAS* mutation**				1
No	1044 (98.96%)	972 (98.88%)	72 (100 %)	
Yes	11 (1.04%)	11 (1.12%)	0 (0%)	
***SH2B3* mutation**				0.606
No	993 (94.12%)	926 (94.20%)	67 (93.06%)	
Yes	62 (5.88%)	57 (5.80%)	5 (6.94%)	
***CSF3R* mutation**				1
No	1050 (99.53%)	978 (99.49%)	72 (100%)	
Yes	5 (0.47%)	5 (0.51%)	0 (0%)	
***NRAS* mutation**				1
No	1041 (98.67%)	970 (98.68%)	71 (98.61%)	
Yes	14 (1.33%)	13 (1.32%)	1 (1.39%)	
***KIT* mutation**				1
No	1054 (99.91%)	982 (99.90%)	72 (100%)	
Yes	1 (0.09%)	1 (0.10%)	0 (0%)	
***BRAF* mutation**				1
No	1051 (99.62%)	979 (99.59%)	72 (100%)	
Yes	4 (0.38%)	4 (0.41%)	0 (0%)	
***FLT3* mutation**				1
No	1053 (99.81%)	981 (99.80%)	72 (100%)	
Yes	2 (0.19%)	2 (0.20%)	0 (0%)	
***PTPN11* mutation**				1
No	1055 (99.43%)	977 (99.39%)	72 (100%)	
Yes	6 (0.57%)	6 (0.61%)	0 (0%)	
***CCND2* mutation**				1
No	1050 (99.53%)	978 (99.49%)	72 (100%)	
Yes	5 (0.47%)	5 (0.51%)	0 (0%)	

Table S6B: MPN patients' cytogenetic and molecular characteristics according to occurrence of venous thrombotic events during follow-up.

	All (n=1055)	Patients with no venous thrombotic event during FU (n=976)	Patients with venous thrombotic events during FU (n=79)	p value
Karyotype, nb (%)				0.172
Normal	99 (9.38%)	94 (9.63%)	5 (6.33%)	
Not normal excluding complex/monosomal	57 (5.40%)	50 (5.12%)	7 (8.86%)	
Complex/monosomal	9 (0.85%)	8 (0.82%)	1 (1.27%)	
***JAK2 V617F* mutation, nb (%)**				**0.011**
No	320 (30.33%)	306 (31.35%)	14 (17.72%)	
Yes	735 (69.67%)	670 (68.85%)	65 (82.28%)	
***JAK2* exon 12 mutation, nb (%)**				
No	1048 (99.34%)	969 (99.28%)	79 (100%)	
Yes	7 (0.66%)	7 (0.72%)	0 (0%)	
***CALR* exon 9 mutation, nb (%)**				0.118
No	880 (83.41%)	809 (82.89%)	71 (89.87%)	
Yes	175 (16.59%)	167 (17.11%)	8 (10.13%)	
***MPL* exon 10 mutation, nb (%)**				0.763
No	1014 (96.11%)	937 (96%)	77 (97.47%)	
Yes	41 (3.89%)	39 (4%)	2 (2.53%)	
Triple negative, nb (%)				0.227
No	958 (90.81%)	883 (90.47%)	75 (94.94%)	
Yes	97 (9.19%)	93 (9.53%)	4 (5.06%)	
Number of additional mutations, median (IQR)	1 [0;2]	1 [0;2]	1 [0;2]	0.87
***TET2* mutation**				0.781
No	814 (77.16%)	754 (77.25%)	60 (75.95%)	
Yes	241 (22.84%)	222 (22.75%)	19 (24.05%)	
***ASXL1* mutation**				0.875
No	878 (83.22%)	811 (83.09%)	67 (84.81%)	
Yes	177 (16.78%)	165 (16.91%)	12 (15.19%)	
***DNMT3A* mutation**				0.763
No	862 (81.71%)	796 (81.56%)	66 (83.54%)	
Yes	193 (18.29%)	180 (18.44%)	13 (16.46%)	
***EZH2* mutation**				0.575
No	1006 (95.36%)	929 (95.18%)	77 (97.47%)	
Yes	49 (4.64%)	47 (4.82%)	2 (2.53%)	
***IDH1* mutation**				**0.043**
No	1044 (98.96%)	968 (99.18%)	76 (96.20%)	
Yes	11 (1.04%)	8 (0.82%)	3 (3.80%)	
***IDH2* mutation**				0.688

No	1032 (97.82%)	955 (97.85%)	77 (97.47%)	
Yes	23 (2.18%)	21 (2.15%)	2 (2.53%)	
***SETBP1* mutation**				1
No	1048 (96.78%)	969 (99.28%)	79 (100%)	
Yes	7 (0.66%)	7 (0.72%)	0 (0%)	
***SRSF2* mutation**				0.71
No	1030 (97.63%)	953 (97.64%)	77 (97.47%)	
Yes	25 (2.37%)	23 (2.36%)	2 (2.53%)	
***U2AF1* mutation**				1
No	1021 (96.78%)	944 (96.72%)	77 (97.47%)	
Yes	34 (3.22%)	32 (3.28%)	2 (2.53%)	
***SF3B1* mutation**				0.541
No	1014 (96.11%)	939 (96.21%)	75 (94.94%)	
Yes	41 (3.89%)	37 (3.79%)	4 (5.06%)	
***ZRSR2* mutation**				0.311
No	1040 (98.58%)	963 (98.67%)	77 (97.47%)	
Yes	15 (1.42%)	13 (1.33%)	2 (2.53%)	
***NFE2* mutation**				0.059
No	1000 (94.79%)	929 (95.18%)	71 (89.87%)	
Yes	55 (5.21%)	47 (4.82%)	8 (10.13%)	
***TP53* mutation**				1
No	999 (94.69%)	924 (94.67%)	75 (94.94%)	
Yes	56 (5.31%)	52 (5.33%)	4 (5.06%)	
***IKZF1* mutation**				0.075
No	1054 (99.91%)	976 (100%)	78 (98.73%)	
Yes	1 (0.09%)	0 (0%)	1 (1.27%)	
***CEBPa* mutation**				1
No	1053 (99.81%)	974 (99.80%)	79 (100%)	
Yes	2 (0.19%)	2 (0.20%)	0 (0%)	
***CUX1* mutation**				0.71
No	1030 (97.63%)	953 (97.64%)	77 (97.47%)	
Yes	25 (2.37%)	23 (2.36%)	2 (2.53%)	
***RUNX1* mutation**				0.609
No	1043 (98.86%)	965 (98.87%)	78 (98.73%)	
Yes	12 (1.14%)	11 (1.13%)	1 (1.27%)	
***ETV6* mutation**				0.141
No	1046 (99.15%)	969 (99.28%)	77 (97.47%)	
Yes	9 (0.85%)	7 (0.72%)	2 (2.53%)	
***CBL* mutation**				0.423
No	1002 (94.98%)	925 (94.77%)	77 (97.47%)	
Yes	53 (5.02%)	51 (5.23%)	2 (2.53%)	
***KRAS* mutation**				0.577
No	1044 (98.96%)	966 (98.98%)	78 (98.73%)	
Yes	11 (1.04%)	10 (1.02%)	1 (1.27%)	

***SH2B3* mutation**				1
No	993 (94.12%)	918 (94.06%)	75 (94.94%)	
Yes	62 (5.88%)	58 (5.94%)	4 (5.06%)	
***CSF3R* mutation**				1
No	1050 (99.53%)	971 (99.49%)	79 (100%)	
Yes	5 (0.47%)	5 (0.51%)	0 (0%)	
***NRAS* mutation**				0.616
No	1041 (98.67%)	962 (98.57%)	79 (100%)	
Yes	14 (1.33%)	14 (1.43%)	0 (0%)	
***KIT* mutation**				1
No	1054 (99.91%)	975 (99.90%)	79 (100%)	
Yes	1 (0.09%)	1 (0.10%)	0 (0%)	
***BRAF* mutation**				1
No	1051 (99.62%)	972 (99.59%)	79 (100%)	
Yes	4 (0.38%)	4 (0.41%)	0 (0%)	
***FLT3* mutation**				1
No	1053 (99.81%)	974 (99.80%)	79 (100%)	
Yes	2 (0.19%)	2 (0.20%)	0 (0%)	
***PTPN11* mutation**				1
No	1055 (99.43%)	970 (99.39%)	79 (100%)	
Yes	6 (0.57%)	6 (0.61%)	0 (0%)	
***CCND2* mutation**				0.323
No	1050 (99.53%)	972 (99.59%)	78 (98.73%)	
Yes	5 (0.47%)	4 (0.41%)	1 (1.27%)	

Table S7A: Univariate and multivariate cause-specific hazard Cox regression model evaluating arterial thrombosis associated factors in patients diagnosed with MPN.

Variables	Univariate analysis*			Multivariate analysis*		
	HR	95% CI	p value	HR	95% CI	p value
Age at MPN diagnosis > 60 years						
No	1					
Yes	3.29	[2.06;5.58]	**0.0001**	2.19	[1.31;3.69]	**0.003**
MPN subtype						
ET	1					
PV	0.94	[0.57;1.54]	0.813			
MF	0.44	[0.14;1.44]	0.174			
MDS/MPN	4.16	[0.56;30.53]	0.161			
MPN unclassified	1.50	[0.36;6.22]	0.577			
Cadiovascular Risk Factor **						
No	1					
Yes	3.94	[2.38;6.54]	**0.001**	3.00	[1.77;5.10]	**0.001**
Arterial thrombosis event anterior to diagnosis or/and at diagnosis						
No	1					
Yes	2.67	[1.51;4.73]	**0.001**	1.81	[1.00;3.25]	**0.046**
Venous thrombosis event anterior to diagnosis or/and at diagnosis						
No	1					
Yes	0.80	[0.37;1.75]	0.579			
Ht (%)	1.01	[0.97;1.05]	0.682			
Platelets (G/L)	1	[0.99;1.00]	0.051			
WBC (G/L)	0.96	[0.87;1.05]	0.394			
JAK 2 V617F mutation						
No	1					
Yes and VAF < 50%	1.21	[0.61;1.74]	0.898			
Yes and VAF ≥ 50%	0.72	[0.37;1.42]	0.349			
CALR mutation						
No	1					
Yes	1.27	[0.72;2.24]	0.415			
MPL mutation						
No	1					
Yes	1.12	[0.35;3.56]	0.847			
Triple negative						
No	1					
Yes	0.45	[0.14;1.43]	0.177			
Number of additionnal mutations	1.12	[0.98;1.29]	0.091			
Epigenetic regulator mutations						
No	1					

Yes	2.16	[1.35;3.45]	**0.001**	1.80	[1.12;2.89]	**0.015**
Spliceosome mutations						
No	1					
Yes	0.17	[0.023;1.22]	0.079			
Signalisation transducer mutations						
No	1					
Yes	1.59	[0.84;3.03]	0.156			
Transcriptionnal factor mutations						
No	1					
Yes	1.48	[0.73;2.98]	0.270			
Adverse prognosis mutations						
No	1					
Yes	0.56	[0.30;1.04]	0.068			

** 9 patients were excluded from the analysis due to absence of diagnosis date (3 patients with ET, 4 patients with PV and 1 patient with unclassified MPN) and absence of arterial thrombosis date (one patient with PV).*

***Cardiovascular risk factors include at least one of the following factors: smoking, arterial hypertension, diabetes or hypercholesterolemia.*

Table S7B: **Univariate and multivariate cause-specific hazard Cox regression model evaluating venous thrombosis associated factors in patients diagnosed with MPN.**

Variables	Univariate analysis*			Multivariate analysis*		
	HR	95% CI	p value	HR	95% CI	p value
Age at MPN diagnosis > 60 years						
No	1					
Yes	1.33	[0.78;2.28]	0.287			
MPN subtype						
ET	1					
PV	1.49	[0.92;2.43]	0.108			
MF	1.70	[0.83;3.49]	0.148			
MDS/MPN	4.42	0.60;32.57]	0.145			
MPN unclassified	2.66	[0.81;8.72]	0.106			
Cadiovascular Risk Factor **						
No	1					
Yes	1.22	[0.78;1.91]	0.378			
Arterial thrombosis event anterior to diagnosis or/and at diagnosis						
No	1					
Yes	1.35	[0.69;2.62]	0.376			
Venous thrombosis event anterior to diagnosis or/and at diagnosis						
No	1			1		
Yes	2.12	[1.24;3.63]	**0.006**	2.17	[1.24;3.76]	**0.006**
Ht (%)	1.00	[0.97;1.04]	0.797			
Platelets (G/L)	0.99	[0.99;1.00]	0.056			
WBC (G/L)	1.01	[0.98;1.06]	0.416			
JAK2 V617F mutation						
No	1			1		
Yes and VAF < 50%	1.21	[0.68;2.13]	0.508	1.05	[0.59;1.89]	0.855
Yes and VAF ≥ 50%	2.12	[1.18;3.81]	**0.011**	2.01	[1.11;3.61]	**0.019**
CALR mutation						
No	1					
Yes	0.52	[0.25;1.07]	0.079			
MPL mutation						
No	1					
Yes	0.65	[0.16;2.66]	0.553			
Triple negative						
No	1					
Yes	0.55	[0.19;1.49]	0.238			
Number of additionnal mutations	0.96	[0.82; 1.12]	0.599			
Epigenetic regulator mutations						
No	1					

Yes	0.95	[0.60;1.51]	0.842
Spliceosome mutations			
No	1		
Yes	1.37	[0.66;2.86]	0.394
Signalisation transducer mutations			
No	1		
Yes	0.53	[0.21;1.31]	0.166
Transcriptionnal factor mutations			
No	1		
Yes	1.50	[0.77;2.92]	0.230
Adverse prognosis mutations			
No	1		
Yes	0.90	[0.54;1.51]	0.685

** 8 patients were excluded from the analysis due to absence of diagnosis date (3 patients with ET, 4 patients with PV and 1 patient with unclassified MPN).*

*** Cardiovascular risk factors include at least one of the following factors: smoking, arterial hypertension, diabetes or hypercholesterolemia.*

Table S8: **External validation cohorts MPN patients' characteristics.**

	Cohort of Brest University Medical Center (n=134)	Cohort of Henri Mondor Hospital (n=190)
Median age	58	60.5
MPN subtype, nb (%)		
ET	85 (63%)	190 (100%)
PV	22 (16.5%)	
MF	25 (19%)	
MPN unclassified	2 (1.5%)	
Median follow-up (years)	4.47	6.81

MPN=Myeloproliferative Neoplasms, ET=Essential Thrombocytopenia, PV=Polycythemia Vera, MF=Myelofibrosis, FU=Follow-up.

Table S9A: MPN patients' cytogenetic and molecular characteristics according to occurrence of "classical" venous thrombotic events during follow-up.

	All (n=1055)	Patients with no "classical" venous thrombotis event during FU (n=1009)	Patients with "classical" venous thrombosis event during FU (n=46)	p value
Karyotype, nb (%)				0.282
Normal	99 (9.38%)	96 (9.51%)	3 (6.52%)	
Not normal excluding complex/monosomal	57 (5.40%)	52 (5.15%)	5 (10.87%)	
Complex/monosomal	9 (0.85%)	9 (0.89%)	0 (0%)	
JAK2 V617F mutation, nb (%)				0.139
No	320 (30.33%)	311 (30.82%)	9 (19.57%)	
Yes	735 (69.67%)	698 (69.18%)	37 (80.43%)	
JAK2 exon 12 mutation, nb (%)				1
No	1048 (99.34%)	1002 (99.31%)	46 (100%)	
Yes	7 (0.66%)	7 (0.69%)	0 (0%)	
CALR mutation, nb (%)				1
No	880 (83.41%)	841 (83.35%)	39 (84.78%)	
Yes	175 (16.59%)	168 (16.65%)	7 (15.22%)	
MPL mutation, nb (%)				1
No	1014 (96.11%)	969 (96.04%)	45 (97.83%)	
Yes	41 (3.89%)	40 (3.96%)	1 (2.17%)	
Triple negative, nb (%)				0.116
No	958 (90.81%)	913 (90.49%)	45 (97.83%)	
Yes	97 (9.19%)	96 (9.51%)	1 (2.17%)	
Number of additional mutations, median (IQR)	1 [0;2]	1 [0;2]	1 [0;2.5]	0.065
TET2 mutation				0.371
No	814 (77.16%)	781 (77.40%)	33 (71.74%)	
Yes	241 (22.84%)	228 (22.60%)	13 (28.26%)	
ASXL1 mutation				0.842
No	878 (83.22%)	840 (83.25%)	38 (82.61%)	
Yes	177 (16.78%)	169 (16.75%)	8 (17.39%)	
DNMT3A mutation				0.437
No	862 (81.71%)	822 (81.47%)	40 (86.96%)	
Yes	193 (18.29%)	187 (18.53%)	6 (13.04%)	
EZH2 mutation				0.719
No	1006 (95.36%)	961 (95.24%)	48 (4.76%)	
Yes	49 (4.64%)	48 (4.76%)	1 (2.17%)	
IDH1 mutation				0.080
No	1044 (98.96%)	1000 (99.11%)	44 (95.65%)	
Yes	11 (1.04%)	9 (0.89%)	2 (4.35%)	

IDH2 mutation				0.265
No	1032 (97.82%)	988 (97.92%)	44 (95.65%)	
Yes	23 (2.18%)	21 (2.08%)	2 (4.35%)	
SETBP1 mutation				1
No	1048 (96.78%)	1002 (99.31%)	46 (100%)	
Yes	7 (0.66%)	7 (0.69%)	0 (0%)	
SRSF2 mutation				0.298
No	1030 (97.63%)	986 (97.72%)	44 (95.65%)	
Yes	25 (2.37%)	23 (2.28%)	2 (4.35%)	
U2AF1 mutation				1
No	1021 (96.78%)	976 (96.73%)	45 (97.83%)	
Yes	34 (3.22%)	33 (3.27%)	1 (2.17%)	
SF3B1 mutation				0.418
No	1014 (96.11%)	971 (96.23%)	43 (93.48%)	
Yes	41 (3.89%)	38 (3.77%)	3 (6.52%)	
ZRSR2 mutation				0.136
No	1040 (98.58%)	996 (98.71%)	44 (95.65%)	
Yes	15 (1.42%)	13 (1.29%)	2 (4.35%)	
NFE2 mutation				**0.028**
No	1000 (94.79%)	960 (95.14%)	40 (86.96%)	
Yes	55 (5.21%)	49 (4.86%)	6 (13.04%)	
TP53 mutation				0.731
No	999 (94.69%)	956 (94.75%)	43 (93.48%)	
Yes	56 (5.31%)	53 (5.25%)	3 (6.52%)	
IKZF1 mutation				**0.044**
No	1054 (99.91%)	1009 (100%)	45 (97.83%)	
Yes	1 (0.09%)	0 (0%)	1 (2.17%)	
CEBPa mutation				1
No	1053 (99.81%)	1007 (99.80%)	46 (100%)	
Yes	2 (0.19%)	2 (0.20%)	0 (0%)	
CUX1 mutation				0.622
No	1030 (97.63%)	984 (97.52%)	46 (100%)	
Yes	25 (2.37%)	25 (2.48%)	0 (0%)	
RUNX1 mutation				1
No	1043 (98.86%)	997 (98.81%)	46 (100%)	
Yes	12 (1.14%)	12 (1.19%)	0 (0%)	
ETV6 mutation				0.332
No	1046 (99.15%)	1001 (99.21%)	45 (97.83%)	
Yes	9 (0.85%)	8 (0.79%)	1 (2.17%)	
CBL mutation				1
No	1002 (94.98%)	958 (94.95%)	44 (95.65%)	
Yes	53 (5.02%)	51 (5.05%)	2 (4.35%)	
KRAS mutation				0.389
No	1044 (98.96%)	999 (99.01%)	45 (97.83%)	

Yes	11 (1.04%)	10 (0.99%)	1 (2.17%)	
SH2B3 mutation				0.748
No	993 (94.12%)	950 (94.15%)	43 (93.48%)	
Yes	62 (5.88%)	59 (5.85%)	3 (6.52%)	
CSF3R mutation				1
No	1050 (99.53%)	1004 (99.50%)	46 (100%)	
Yes	5 (0.47%)	5 (0.50%)	0 (0%)	
NRAS mutation				1
No	1041 (98.67%)	995 (98.61%)	46 (100%)	
Yes	14 (1.33%)	14 (1.39%)	0 (0%)	
KIT mutation				1
No	1054 (99.91%)	1008 (99.90%)	46 (100%)	
Yes	1 (0.09%)	1 (0.10%)	0 (0%)	
BRAF mutation				1
No	1051 (99.62%)	1005 (99.60%)	46 (100%)	
Yes	4 (0.38%)	4 (0.41%)	0 (0%)	
FLT3 mutation				1
No	1053 (99.81%)	1007 (99.80%)	46 (100%)	
Yes	2 (0.19%)	2 (0.20%)	0 (0%)	
PTPN11 mutation				1
No	1049 (99.43%)	1003 (99.41%)	46 (100%)	
Yes	6 (0.57%)	6 (0.59%)	0 (0%)	
CCND2 mutation				0.200
No	1050 (99.53%)	1005 (99.60%)	45 (97.83%)	
Yes	5 (0.47%)	4 (0.40%)	1 (2.17%)	

Table S9B: MPN patients' cytogenetic and molecular characteristics according to occurrence of splanchnic thrombotic events during follow-up.

	All (n=1055)	Patients with no splanchnic thrombotis event during FU (n=1027)	Patients with splanchnic thrombotis events during FU (n=28)	p value
Karyotype, nb (%)				0.208
Normal	99 (9.38%)	97 (9.44%)	2 (7.14%)	
Not normal excluding complex/monosomal	57 (5.40%)	55 (5.35%)	2 (7.14%)	
Complex/monosomal	9 (0.85%)	8 (7.79%)	1 (3.57%)	
JAK2 V617F mutation, nb (%)				0.063
No	320 (30.33%)	316 (30.77%)	4 (14.29%)	
Yes	735 (69.67%)	711 (69.23%)	24 (85.71%)	
JAK2 exon 12 mutation, nb (%)				1
No	1048 (99.34%)	1020 (99.32%)	28 (100%)	
Yes	7 (0.66%)	7 (0.68%)	0 (0%)	
CALR mutation, nb (%)				0.070
No	880 (83.41%)	853 (83.06%)	27 (96.43%)	
Yes	175 (16.59%)	174 (16.94%)	1 (3.57%)	
MPL mutation, nb (%)				1
No	1014 (96.11%)	987 (96.11%)	27 (96.43%)	
Yes	41 (3.89%)	40 (3.89%)	1 (3.57%)	
Triple negative, nb (%)				1
No	958 (90.81%)	932 (90.75%)	26 (92.86%)	
Yes	97 (9.19%)	95 (9.25%)	2 (7.14%)	
Number of additional mutations, median (IQR)	1 [0;2]	1 [0;2]	1 [0;2]	0.87
TET2 mutation				1
No	814 (77.16%)	792 (77.12%)	22 (78.57%)	
Yes	241 (22.84%)	235 (22.88%)	6 (21.43%)	
ASXL1 mutation				1
No	878 (83.22%)	854 (83.15%)	24 (85.71%)	
Yes	177 (16.78%)	173 (16.85%)	4 (14.29%)	
DNMT3A mutation				0.623
No	862 (81.71%)	840 (81.79%)	22 (78.57%)	
Yes	193 (18.29%)	187 (18.21%)	6 (21.43%)	
EZH2 mutation				0.575
No	1006 (95.36%)	979 (95.33%)	27 (96.43%)	
Yes	49 (4.64%)	48 (4.67%)	1 (3.57%)	
IDH1 mutation				0.257
No	1044 (98.96%)	1017 (99.03%)	27 (96.43%)	
Yes	11 (1.04%)	10 (0.97%)	1 (3.57%)	
IDH2 mutation				1

No	1032 (97.82%)	1004 (97.76%)	28 (100%)	
Yes	23 (2.18%)	23 (2.24%)	0 (0%)	
SETBP1 mutation				1
No	1048 (96.78%)	1020 (99.32%)	28 (100%)	
Yes	7 (0.66%)	7 (0.68%)	0 (0%)	
SRSF2 mutation				1
No	1030 (97.63%)	1002 (97.57%)	28 (100%)	
Yes	25 (2.37%)	25 (2.43%)	0 (0%)	
U2AF1 mutation				0.605
No	1021 (96.78%)	994 (96.79%)	27 (96.43%)	
Yes	34 (3.22%)	33 (3.21%)	1 (3.57%)	
SF3B1 mutation				1
No	1014 (96.11%)	987 (96.11%)	27 (96.43%)	
Yes	41 (3.89%)	40 (3.89%)	1 (3.57%)	
ZRSR2 mutation				1
No	1040 (98.58%)	1012 (98.54%)	28 (100%)	
Yes	15 (1.42%)	15 (1.42%)	0 (0%)	
NFE2 mutation				0.654
No	1000 (94.79%)	974 (94.84%)	26 (92.86%)	
Yes	55 (5.21%)	53 (5.16%)	2 (7.14%)	
TP53 mutation				0.395
No	999 (94.69%)	971 (94.55%)	28 (100%)	
Yes	56 (5.31%)	56 (5.45%)	0 (0%)	
IKZF1 mutation				1
No	1054 (99.91%)	1026 (99.90%)	28 (100%)	
Yes	1 (0.09%)	1 (0.10%)	0 (0%)	
CEBPa mutation				1
No	1053 (99.81%)	1025 (99.81%)	28 (100%)	
Yes	2 (0.19%)	2 (0.19%)	0 (0%)	
CUX1 mutation				0.140
No	1030 (97.63%)	1004 (97.76%)	26 (92.86%)	
Yes	25 (2.37%)	23 (2.24%)	2 (7.14%)	
RUNX1 mutation				0.277
No	1043 (98.86%)	1016 (98.93%)	27 (96.43%)	
Yes	12 (1.14%)	11 (1.07%)	1 (3.57%)	
ETV6 mutation				0.216
No	1046 (99.15%)	1019 (99.22%)	27 (96.43%)	
Yes	9 (0.85%)	8 (0.78%)	1 (3.57%)	
CBL mutation				0.394
No	1002 (94.98%)	974 (94.84%)	28 (100%)	
Yes	53 (5.02%)	53 (5.16%)	0 (0%)	
KRAS mutation				1
No	1044 (98.96%)	1016 (98.93%)	28 (100%)	
Yes	11 (1.04%)	11 (1.04%)	0 (0%)	

SH2B3 mutation				1
No	993 (94.12%)	966 (94.06%)	27 (96.43%)	
Yes	62 (5.88%)	61 (5.94%)	1 (3.57%)	
CSF3R mutation				1
No	1050 (99.53%)	1022 (99.51%)	28 (100%)	
Yes	5 (0.47%)	5 (0.49%)	0 (0%)	
NRAS mutation				1
No	1041 (98.67%)	1013 (98.64%)	28 (100%)	
Yes	14 (1.33%)	14 (1.36%)	0 (0%)	
KIT mutation				1
No	1054 (99.91%)	1026 (99.90%)	28 (100%)	
Yes	1 (0.09%)	1 (0.10%)	0 (0%)	
BRAF mutation				1
No	1051 (99.62%)	1023 (99.61%)	28 (100%)	
Yes	4 (0.38%)	4 (0.39%)	0 (0%)	
FLT3 mutation				1
No	1053 (99.81%)	1025 (99.81%)	28 (100%)	
Yes	2 (0.19%)	2 (0.19%)	0 (0%)	
PTPN11 mutation				1
No	1049 (99.43%)	1021 (99.42%)	28 (100%)	
Yes	6 (0.57%)	6 (0.58%)	0 (0%)	
CCND2 mutation				0.323
No	1050 (99.53%)	1022 (99.51%)	28 (100%)	
Yes	5 (0.47%)	5 (0.49%)	0 (0%)	

Table S9C: MPN patients' cytogenetic and molecular characteristics according to occurrence of cerebral venous thrombotic events during follow-up.

	All (n=1055)	Patients with no cerebral venous thrombosis event during FU (n=1050)	Patients with cerebral venous thrombosis event during FU (n=5)	p value
Karyotype, nb (%)				NA
Normal	99 (9.38%)	99 (9.42%)	0 (0%)	
Not normal excluding complex/monosomal	57 (5.40%)	57 (5.43%)	0 (0%)	
Complex/monosomal	9 (0.85%)	9 (0.86%)	0 (0%)	
JAK2 V617F mutation, nb (%)				1
No	320 (30.33%)	319 (30.38%)	1 (20%)	
Yes	735 (69.67%)	731 (69.62%)	4 (80%)	
JAK2 exon 12 mutation, nb (%)				1
No	1048 (99.34%)	1043 (99.33%)	5 (100%)	
Yes	7 (0.66%)	7 (0.67%)	0 (0%)	
CALR mutation, nb (%)				1
No	880 (83.41%)	875 (83.33%)	5 (100%)	
Yes	175 (16.59%)	175 (16.67%)	0 (0%)	
MPL mutation, nb (%)				1
No	1014 (96.11%)	1009 (96.10%)	5 (100%)	
Yes	41 (3.89%)	41 (3.90%)	0 (0%)	
Triple negative, nb (%)				0.383
No	958 (90.81%)	954 (90.86%)	4 (80%)	
Yes	97 (9.19%)	96 (9.14%)	1 (20%)	
Number of additional mutations, median (IQR)	1 [0;2]	1 [0;2.5]	1 [0;2]	0.15
TET2 mutation				0.594
No	814 (77.16%)	809 (77.05%)	5 (100%)	
Yes	241 (22.84%)	241 (22.95%)	0 (0%)	
ASXL1 mutation				0.597
No	878 (83.22%)	873 (83.14%)	5 (100%)	
Yes	177 (16.78%)	177 (16.86%)	0 (0%)	
DNMT3A mutation				1
No	862 (81.71%)	858 (81.71%)	4 (80%)	
Yes	193 (18.29%)	192 (18.29%)	1 (20%)	
EZH2 mutation				1
No	1006 (95.36%)	1001 (95.33%)	5 (100%)	
Yes	49 (4.64%)	49 (4.67%)	0 (0%)	
IDH1 mutation				1
No	1044 (98.96%)	1039 (98.95%)	5 (100%)	
Yes	11 (1.04%)	11 (1.05%)	0 (0%)	

IDH2 mutation				1
No	1032 (97.82%)	1027 (97.81%)	5 (100%)	
Yes	23 (2.18%)	23 (2.19%)	0 (0%)	
SETBP1 mutation				1
No	1048 (96.78%)	1043 (99.33%)	5 (100%)	
Yes	7 (0.66%)	7 (0.67%)	0 (0%)	
SRSF2 mutation				1
No	1030 (97.63%)	1025 (97.62%)	5 (100%)	
Yes	25 (2.37%)	25 (2.38%)	0 (0%)	
U2AF1 mutation				1
No	1021 (96.78%)	1016 (96.76%)	5 (100%)	
Yes	34 (3.22%)	34 (3.24%)	0 (0%)	
SF3B1 mutation				1
No	1014 (96.11%)	1009 (96.10%)	5 (100%)	
Yes	41 (3.89%)	41 (3.90%)	0 (0%)	
ZRSR2 mutation				1
No	1040 (98.58%)	1035 (98.57%)	5 (100%)	
Yes	15 (1.42%)	15 (1.43%)	0 (0%)	
NFE2 mutation				1
No	1000 (94.79%)	995 (94.76%)	5 (100%)	
Yes	55 (5.21%)	55 (5.24%)	0 (0%)	
TP53 mutation				0.239
No	999 (94.69%)	995 (94.76%)	4 (80%)	
Yes	56 (5.31%)	55 (5.24%)	1 (20%)	
IKZF1 mutation				1
No	1054 (99.91%)	1049 (99.90%)	5 (100%)	
Yes	1 (0.09%)	1 (0.10%)	0 (0%)	
CEBPa mutation				1
No	1053 (99.81%)	1048 (99.81%)	5 (100%)	
Yes	2 (0.19%)	2 (0.19%)	0 (0%)	
CUX1 mutation				1
No	1030 (97.63%)	1025 (97.62%)	5 (100%)	
Yes	25 (2.37%)	25 (2.38%)	0 (0%)	
RUNX1 mutation				1
No	1043 (98.86%)	1038 (98.86%)	5 (100%)	
Yes	12 (1.14%)	12 (1.14%)	0 (0%)	
ETV6 mutation				1
No	1046 (99.15%)	1041 (99.14%)	5 (100%)	
Yes	9 (0.85%)	9 (0.86%)	0 (0%)	
CBL mutation				1
No	1002 (94.98%)	997 (94.95%)	5 (100%)	
Yes	53 (5.02%)	53 (5.05%)	0 (0%)	
KRAS mutation				1
No	1044 (98.96%)	1039 (98.95%)	5 (100%)	

Yes	11 (1.04%)	11 (1.05%)	0 (0%)	
SH2B3 mutation				1
No	993 (94.12%)	988 (94.10%)	5 (100%)	
Yes	62 (5.88%)	62 (5.90%)	0 (0%)	
CSF3R mutation				1
No	1050 (99.53%)	1045 (99.52%)	5 (100%)	
Yes	5 (0.47%)	5 (0.48%)	0 (0%)	
NRAS mutation				1
No	1041 (98.67%)	1036 (98.67%)	5 (100%)	
Yes	14 (1.33%)	14 (1.33%)	0 (0%)	
KIT mutation				1
No	1054 (99.91%)	1049 (99.90%)	5 (100%)	
Yes	1 (0.09%)	1 (0.10%)	0 (0%)	
BRAF mutation				1
No	1051 (99.62%)	1046 (99.62%)	5 (100%)	
Yes	4 (0.38%)	4 (0.38%)	0 (0%)	
FLT3 mutation				1
No	1053 (99.81%)	1048 (99.81%)	5 (100%)	
Yes	2 (0.19%)	2 (0.19%)	0 (0%)	
PTPN11 mutation				1
No	1049 (99.43%)	1044 (99.43%)	5 (100%)	
Yes	6 (0.57%)	6 (0.57%)	0 (0%)	
CCND2 mutation				1
No	1050 (99.53%)	1045 (99.52%)	5 (100%)	
Yes	5 (0.47%)	5 (0.48%)	0 (0%)	

Table S10A: Univariate and multivariate cause-specific hazard Cox regression model evaluating classical* venous thrombosis associated factors in patients diagnosed with MPN.

Variables	Univariate analysis**			Multivariate analysis**		
	HR	95% CI	pval	HR	95% CI	pval
Age at MPN diagnosis						
No	1			1		
Yes	1.96	[1.08;3.56]	0.027	1.70	[1.05;3.13]	**0.043**
MPN subtype						
ET	1					
PV	1.54	[0.84;2.85]	0.108			
MF	1.17	[0.39;3.45]	0.780			
MDS/MPN	8.03	[0.96;60.70]	0.053			
MPN unclassified	NA	NA	NA			
Cardiovascular Risk Factor ***						
No	1					
Yes	1.16	[0.64;2.09]	0.622			
Arterial thrombosis event anterior to diagnosis or/and at diagnosis						
No	1					
Yes	1.35	[0.69;2.62]	0.376			
Classical venous thrombosis event anterior to diagnosis or/and at diagnosis						
No	1			1		
Yes	6.07	[2.83;13.04]	**0.001**	5.43	[2.51;11.76]	**0.001**
Ht (%)	1.01	[0.97;1.07]	0.531			
Platelets (G/L)	0.99	[0.99;1.00]	0.443			
WBC (G/L)	0.97	[0.89;1.06]	0.543			
JAK2 V617F mutation						
No	1					
Yes and VAF < 50%	1.10	[0.51;2.35]	0.808			
Yes and VAF ≥ 50%	2.28	[1.07;4.82]	**0.032**			
CALR mutation						
No	1					
Yes	0.85	[0.38;1.90]	0.689			
MPL mutation						
No	1					
Yes	0.57	[0.08;4.15]	0.581			
Triple negative						
No	1					
Yes	0.23	[0.03;1.65]	0.142			
Number of additionnal mutations	1.04	[0.86; 1.26]	0.696			
Epigenetic regulator mutations						

No	1		
Yes	1.01	[0.55;1.84]	0.973
Spliceosome mutations			
No	1		
Yes	1.87	[0.79;4.42]	0.153
Signaling mutations			
No	1		
Yes	0.77	[0.27;2.14]	0.612
Transcription factor mutations			
No	1		
Yes	1.51	[0.64;3.57]	0.343
Adverse prognosis mutations			
No	1		
Yes	1.63	[0.90;2.97]	0.110

**Classical venous thrombosis design limb venous thrombosis and pulmonary embolism.*

*** 8 patients were excluded from the analysis due to absence of diagnosis date (3 patients with ET, 4 patients with PV and 1 patient with unclassified MPN).*

**** Cardiovascular risk factors include at least one of the following factors: smoking, arterial hypertension, diabetes or hypercholesterolemia.*

Table S10B: Univariate cause-specific hazard Cox regression model evaluating splanchnic thrombosis associated factors in patients diagnosed with MPN.

Variables	Univariate analysis*		
	HR	**95% CI**	**pval**
Age at MPN diagnosis			
No	1		
Yes	0.70	[0.24;2.04]	0.516
MPN subtype			
ET	1		
PV	1.50	[0.64;3.54]	0.350
MF	2.99	[0.90;8.37]	0.063
MDS/MPN	NA	NA	NA
MPN unclassified	NA	NA	NA
Cardiovascular Risk Factor **			
No	1		
Yes	1.17	[0.56;2.50]	0.667
Arterial thrombosis event anterior to diagnosis or/and at diagnosis			
No	1		
Yes	1.98	[0.75;5.23]	0.164

Splanchnic thrombosis event anterior to diagnosis or/and at diagnosis			
No	1		
Yes	1.45	[0.44;4.81]	0.544
Ht (%)	0.97	[0.92;1.04]	0.433
Platelets (G/L)	0.99	[0.99;1.00]	0.053
WBC (G/L)	1.04	[0.99;1.08]	0.055
JAK2 V617F mutation			
No	1		
Yes and VAF < 50%	1.42	[0.53;3.79]	0.480
Yes and VAF ≥ 50%	2.36	[0.86;6.53]	0.095
CALR mutation			
No	1		
Yes	0.17	[0.02;1.28]	0.086
MPL mutation			
No	1		
Yes	0.94	[0.13;6.91]	0.951
Triple negative			
No	1		
Yes	0.79	[0.19;3.37]	0.760
Number of additionnal mutations	0.89	[0.67; 1.19]	0.431
Epigenetic regulator mutations			
No	1		
Yes	0.97	[0.45;2.10]	0.934
Spliceosome mutations			
No	1		
Yes	0.90	[0.21;3.78]	0.882
Signaling mutations			
No	1		
Yes	0.30	[0.04;2.17]	0.231
Transcription factor mutations			
No	1		
Yes	1.75	[0.61;5.05]	0.299
Adverse prognosis mutations			
No	1		
Yes	0.73	[0.30;1.80]	0.496

** 8 patients were excluded from the analysis due to absence of diagnosis date (3 patients with ET, 4 patients with PV and 1 patient with unclassified MPN).*

*** Cardiovascular risk factors include at least one of the following factors: smoking, arterial hypertension, diabetes or hypercholesterolemia.*

Table S10C: Univariate cause-specific hazard Cox regression model evaluating cerebral venous thrombosis associated factors in patients diagnosed with MPN.

Variables	Univariate analysis*		
	HR	**95% CI**	**pval**
Age at MPN diagnosis			
No	1		
Yes	0.89	[0.09;7.99]	0.915
MPN subtype			
ET	1		
PV	0.67	[0.061;7.43]	0.747
MF	NA	NA	NA
MDS/MPN	NA	NA	NA
MPN unclassified	NA	NA	NA
Cardiovascular Risk Factor **			
No	1		
Yes	2.23	[0.37;13.40]	0.377
Arterial thrombosis event anterior to diagnosis or/and at diagnosis			
No	1		
Yes	2.17	[0.24;19.42]	0.488
Cerebral venous thrombosis event anterior to diagnosis or/and at diagnosis			
No	1		
Yes	1.98	[0.05;12.08]	0.072
Ht (%)	1.07	[0.93;1.25]	0.313
Platelets (G/L)	0.99	[0.99;1.00]	0.752
WBC (G/L)	0.98	[0.76;1.25]	0.846
JAK2 V617F mutation			
No	1		
Yes and VAF < 50%	1.02	[0.17;6.12]	0.980
Yes and VAF ≥ 50%	NA	NA	NA
CALR mutation			
No	1		
Yes	NA	NA	NA
MPL mutation			
No	1		
Yes	NA	NA	NA
Triple negative			
No	1		
Yes	2.63	[0.29;23.52]	0.388
Number of additionnal mutations	0.44	[0.12; 1.55]	0.199

Epigenetic regulator mutations			
No	1		
Yes	0.44	[0.04;3.89]	0.456
Spliceosome mutations			
No	1		
Yes	NA	NA	NA
Signaling mutations			
No	1		
Yes	NA	NA	NA
Transcription factor mutations			
No	1		
Yes	NA	NA	NA
Adverse prognosis mutations			
No	1		
Yes	NA	NA	NA

** 8 patients were excluded from the analysis due to absence of diagnosis date (3 patients with ET, 4 patients with PV and 1 patient with unclassified MPN).*

*** Cardiovascular risk factors include at least one of the following factors: smoking, arterial hypertension, diabetes or hypercholesterolemia.*

Table S11: Preventive MPN treatments received according to occurrence of arterial or venous thrombotic events during follow-up.

Variables		According to arterial thrombosis			According to venous thrombosis		
	All (n=1055)	No arterial thrombotic event during FU (n=983)	Arterial thrombotic events during FU (n=72)	p value	No venous thrombotic event during FU (n=976)	Venous thrombotic events during FU (n=79)	p value
Antiplatelet drugs prior to event during FU, nb (%)				**0.014**			0.432
No	291 (27.58%)	280 (28.48%)	11 (15.28%)		266 (27.25%)	25 (31.65%)	
Yes	764 (72.42%)	703 (71.52%)	61 (84.72%)		710 (72.75%)	54 (68.35%)	
Anticoagulants prior to during FU, nb (%)				0.748			**0.0001**
No	873 (82.75%)	812 (82.60%)	61 (84.72%)		853 (87.40%)	20 (25.32%)	
Yes	182 (17.25%)	171 (17.40%)	11 (15.28%)		123 (12.60%)	59 (74.68%)	
Cytoreductive treatment prior to event during FU, nb (%)				0.881			**0.002**
No	222 (21.04%)	208 (21.16%)	14 (19.44%)		194 (19.88%)	28 (35.44%)	
Yes	833 (78.96%)	775 (78.84%)	58 (80.56%)		782 (80.12%)	51 (64.56%)	
Hydroxyurea prior to event during FU, nb (%)				**0.044**			**0.016**
No	399 (37.82%)	380 (38.66%)	19 (26.39%)		359 (36.78%)	39 (49.37%)	
Yes	656 (62.18%)	603 (61.34%)	55 (73.61%)		617 (63.22%)	40 (50.63%)	
Interferon-alpha prior to event during FU, nb (%)				**0.013**			**0.0001**
No	710 (67.30%)	652 (66.33%)	58 (80.56%)		637 (65.27%)	73 (92.41%)	
Yes	345 (32.70%)	331 (33.67%)	14 (19.44%)		339 (34.73%)	6 (7.59%)	
Ruxolitinib prior to event during FU, nb (%)				**0.0001**			**0.027**
No	879 (83.32%)	808 (82.20%)	71 (98.61%)		806 (82.58%)	73 (92.41%)	
Yes	176 (16.68%)	175 (17.80%)	1 (1.39%)		170 (17.42%)	6 (7.59%)	
Other cytoreductive treatment prior to event during FU*, nb (%)				0.126			0.377
No	849 (80.47%)	786 (79.96%)	63 (87.50%)		782 (80.12%)	67 (84.91%)	
Yes	206 (19.53%)	197 (20.04%)	9 (12.50%)		194 (19.88%)	12 (15.19%)	

** Other cytoreductive treatment included Anagrelide, Pipobroman, chemotherapy, Revlimid, steroids, phosphore 32, hypomethylating agents, other JAK inhibitor and Panobinostat.*

nb=Number of patients, FU=Follow-up.

Table S12A: **Univariate cause-specific hazard Cox regression model evaluating the impact of preventive MPN cytoreductive treatments stratified by ARTS score, on arterial thrombosis risk.**

Variables	Univariate analysis*		
	HR	**95% CI**	**p value**
Hydroxyurea prior to event during FU			
No	1		
Yes	1.05	[0.60;1.83]	0.863
Interferon-alpha prior to event during FU			
No	1		
Yes	0.41	[0.23;0.74]	**0.003**
Ruxolitinib prior to event during FU			
No	1		
Yes	0.05	[0.01;0.34]	**0.003**

ARTS=ARterial Thrombosis Score, HR=Hazard Ratio, FU=Follow-up.

** 9 patients were excluded from the analysis due to absence of diagnosis date (3 patients with ET, 4 patients with PV and 1 patient with unclassified MPN) and absence of arterial thrombosis date (one patient with PV).*

Table S12B: **Univariate cause-specific hazard Cox regression model evaluating the impact of preventive MPN cytoreductive treatments stratified by VETS score, on venous thrombosis risk.**

Variables	Univariate analysis*		
	HR	**95% CI**	**p value**
Hydroxyurea prior to event during FU			
No	1		
Yes	0.42	[0.27;0.66]	**<0.001**
Interferon-alpha prior to event during FU			
No	1		
Yes	0.17	[0.09;0.35]	**<0.001**
Ruxolitinib prior to event during FU			
No	1		
Yes	0.41	[0.20;0.86]	**0.018**

VETS=VEnous Thrombosis Score, HR=Hazard Ratio, FU=Follow-up.

** 8 patients were excluded from the analysis due to absence of diagnosis date (3 patients with ET, 4 patients with PV and 1 patient with unclassified MPN).*

Table S13: Outcome of patients diagnosed with MPN according to occurrence of arterial or venous thrombotic events during follow-up.

	All (n=1055)	Patients with arterial thrombotic events during FU (n=72)	Patients with venous thrombotic events during FU (n=79)	p value
MF transformation during FU, nb (%)				0.555
No	737 (69.86%)	55 (79.71%)	51 (73.91%)	
Yes	158 (15.07%)	14 (20.29%)	18 (26.09%)	
AML/MDS transformation during FU, nb (%)				**0.048**
No	994 (94.21%)	64 (88.89%)	77 (97.47%)	
Yes	61 (5.78%)	8 (11.11%)	2 (2.53%)	
Death during FU, nb (%)				0.630
No	946 (89.67%)	61 (84.72%)	70 (88.61%)	
Yes	109 (10.33%)	11 (15.28%)	9 (11.39%)	
Cause of death, nb (%)				0.116
Arterial thrombotic event	2 (0.19%)	2 (2.78%)	0 (0%)	
Venous thrombotic event	2 (0.19%)	0 (0%)	2 (2.53%)	
Hemorrhagic event	10 (0.95%)	0 (0%)	1 (1.27%)	
Global condition deterioration	7 (0.66%)	2 (2.78%)	2 (2.53%)	
Pulmonary or cerebral leukostasis	9 (0.85%)	1 (1.39%)	1 (1.27%)	
HSCT	14 (1.33%)	0 (0%)	0 (0%)	
Infection	32 (3.03%)	4 (5.56%)	0 (0%)	
Solid cancer	8 (0.76%)	0 (0%)	1 (1.27%)	
Other	5 (0.47%)	0 (0%)	1 (1.27%)	
Undetermined	20 (1.90%)	2 (2.78%)	1 (1.27%)	
MPN state at death, nb (%)				0.642
Chronic initial MPN	70 (6.64%)	6 (8.33%)	7 (8.86%)	
MF transformation	9 (0.85%)	1 (1.39%)	1 (1.27%)	
AML/MDS transformation	30 (2.84%)	4 (5.56%)	1 (1.27%)	

FU=Follow-up, nb=number, MPN=Myeloproliferative Neoplasms, MF=Myelofibrosis, MDS=Myelodysplastic Syndrom, AML=Acute Myeloid Leukemia, HSCT=Hematopoietic Stem Cell Transplantation.

Supplemental figures

Supplemental figure legends:

Figure S1: Study population flow chart.

Study flowchart representing our MPN cohort, including all consecutive patients with appropriate diagnosis.

Figure S2: **Type of arterial and venous thrombotic events in PV, ET and MF patients.**

A. Type of arterial and venous thrombotic events occurred prior to and/or at diagnosis of PV, ET or MF.

B. Type of arterial and venous thrombotic events occurred during PV, ET or MF patients' follow-up.

PV=Polycythemia Vera, ET=Essential Thrombocythemia, MF=Myelofibrosis, AMI=Acute Myocardial Infarction, TIA=Transient Ischemic Attack.

Figure S3: **Absolute ARterial Thrombosis Score (ARTS) in patients diagnosed with MPN.**

Cumulative incidence of arterial thrombosis curves according to absolute arterial risk score.

Figure S4: **The two-tiered conventional risk score and to the International Prognostic Score of Thrombosis for Essential Thrombocythemia revised (IPSET) for arterial thrombosis in the two external validation cohorts.**

A. Cumulative incidence of arterial thrombosis according to the two-tiered conventional risk score in the first external validation cohort from Brest University Medical Center compared. **B.** Cumulative incidence of arterial thrombosis according to the two-tiered conventional risk score and to the International Prognostic Score of Thrombosis for Essential Thrombocythemia revised (IPSET revised).

4 patients of Henri Mondor cohort were excluded from the arterial thrombosis analysis due to absence of diagnosis date

MPN=Myeloproliferative Neoplasm, CV=Cardiovascular.

**Cardiovascular risk factors include at least one of the following factors: smoking, arterial hypertension, diabetes or hypercholesterolemia.*

Figure S5: **Absolute VEnous Thrombosis Score (VETS) in patients diagnosed with MPN compared to the two-tiered conventional risk.**

- **A.** Cumulative incidence of venous thrombosis curves according to VEnous Thrombosis Score (VETS).
- **B.** Cumulative incidence of venous thrombosis curves according to the two-tiered conventional risk.

Figure S6: **Clinical, biological and molecular factors associated with classical* venous thrombosis in MPN.**

Clinical, biological and molecular factors associated with classical venous thrombosis using a cause-specific hazard Cox regression model. Variables highlighted in red are significantly associated in the univariable analysis, a red star highlights independently associated variables within the multivariable analysis.

MPN=Myeloproliferative Neoplasm, PV=Polycythemia Vera, ET=Essential Thrombocythemia, MF=Myelofibrosis, MDS=Myelodysplastic Syndrom, WBC=White Blood Count, VAF=Variant Allelic Fraction.

**Classical venous thrombosis designed limb venous thrombosis and pulmonary embolism*

***CV risk factors include at least one of the following factors: smoking, arterial hypertension, diabetes or hypercholesterolemia.*

Figure S7: **Cytoreductive treatments prior to thrombotic event associated with arterial or venous thrombosis prevention in MPN.**

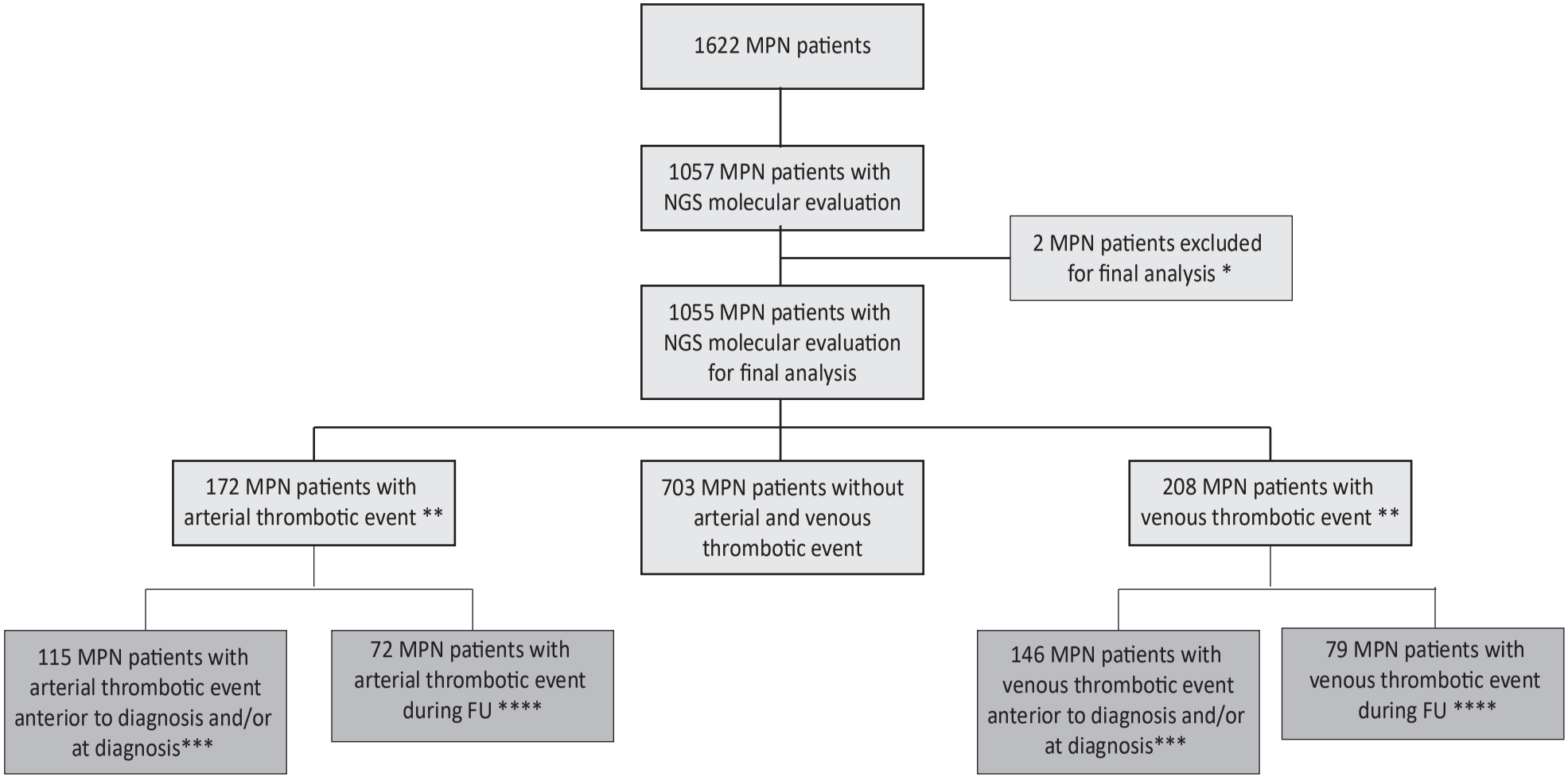
A. Cytoreductive treatments prior to thrombotic event associated with arterial thrombosis using a cause-specific hazard Cox regression model stratified by ARTS (ARterial Thrombosis Score). **B.** Cytoreductive treatments prior to thrombotic event associated with venous thrombosis using a cause-specific hazard Cox regression model stratified by VETS (Venous Thrombosis Score). Variables highlighted in red are significantly associated in the univariable analysis.

Figure S8: **Outcome of patients diagnosed with arterial or venous thrombotic events during MPN follow-up.**

A. Causes of death and MPN disease state at time of death **B.** Kaplan-Meier curves of AML/MDS-transformation free survival, MF-transformation free survival, and OS in patients diagnosed with arterial or venous thrombotic events during MPN follow-up.

OS=Overall Survival, MPN=Myeloproliferative Neoplasms, MF=Myelofibrosis, AML=Acute Myeloid Leukemia, MDS=Myelodysplastic Syndrom.

Figure S1



* 2 MPN patients with both arterial and venous thrombosis events during FU
** 28 MPN patients with both arterial and venous thrombotic events
*** 11 MPN patients with both arterial and venous thrombotic events anterior to diagnosis and/or at diagnosis
**** 15 MPN patients with both anterior and posterior arterial thrombotic events and 17 MPN patients with both anterior and posterior venous thrombotic events

Figure S2

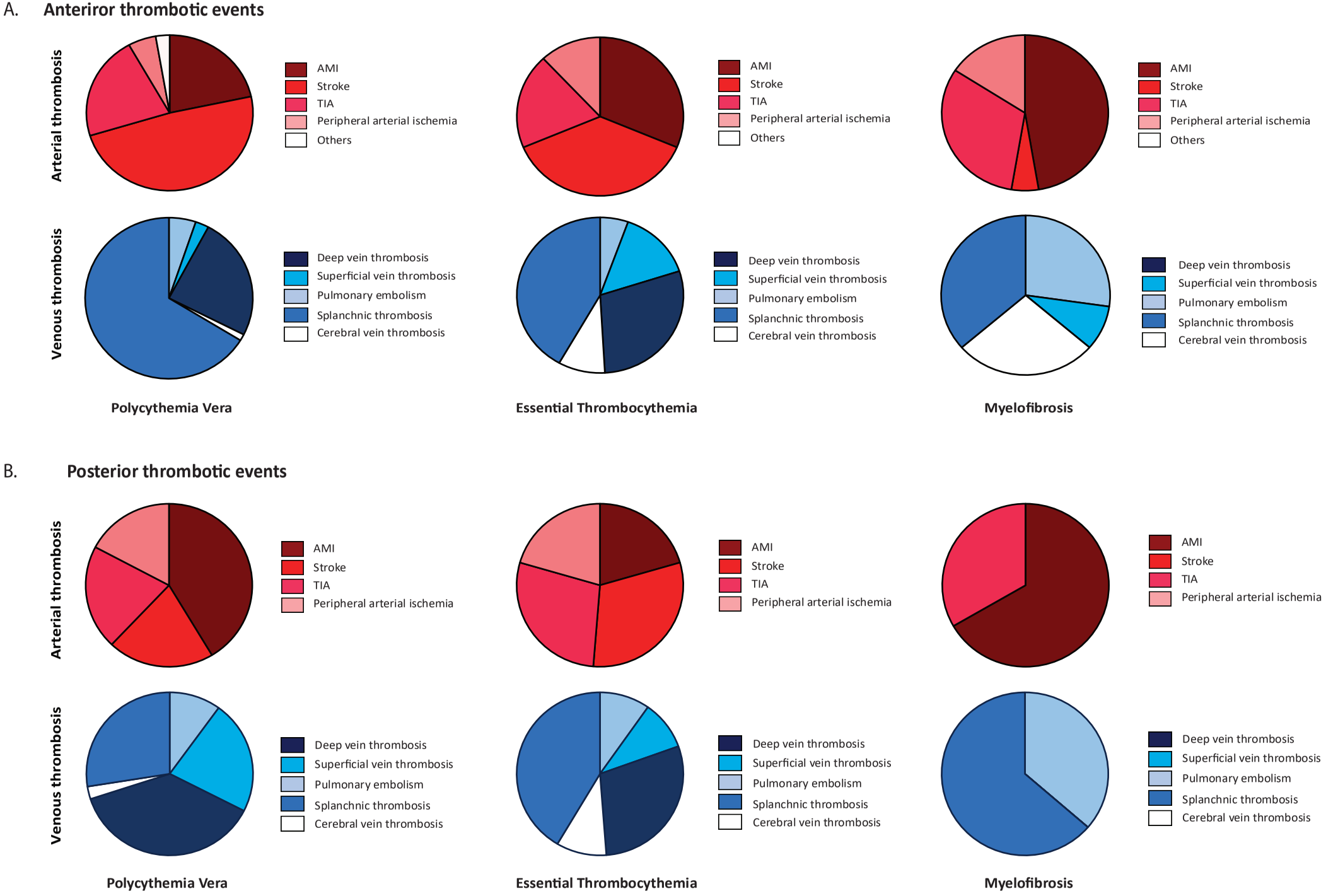
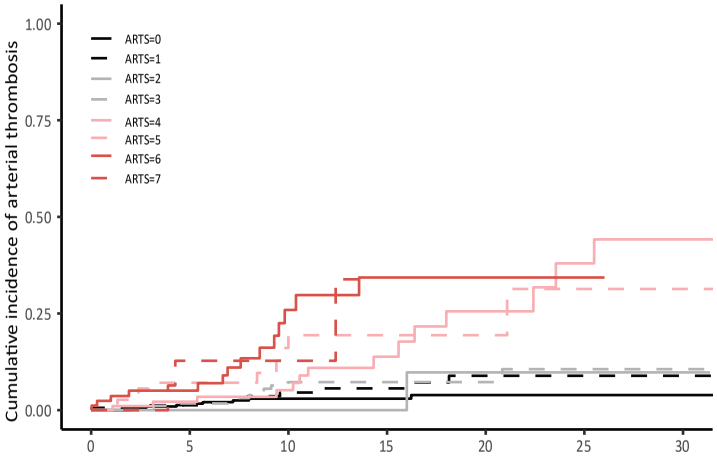

A.
Anteriror thrombotic events
Arterial thrombosis
AMI
Stroke
TIA
Peripheral arterial ischemia
Others
Venous thrombosis
Deep vein thrombosis
Superficial vein thrombosis
Pulmonary embolism
Splanchnic thrombosis
Cerebral vein thrombosis
Polycythemia Vera
Essential Thrombocythemia
Myelofibrosis
B.
Posterior thrombotic events
Arterial thrombosis
AMI
Stroke
TIA
Peripheral arterial ischemia
Venous thrombosis
Deep vein thrombosis
Superficial vein thrombosis
Pulmonary embolism
Splanchnic thrombosis
Cerebral vein thrombosis
Polycythemia Vera
Essential Thrombocythemia
Myelofibrosis

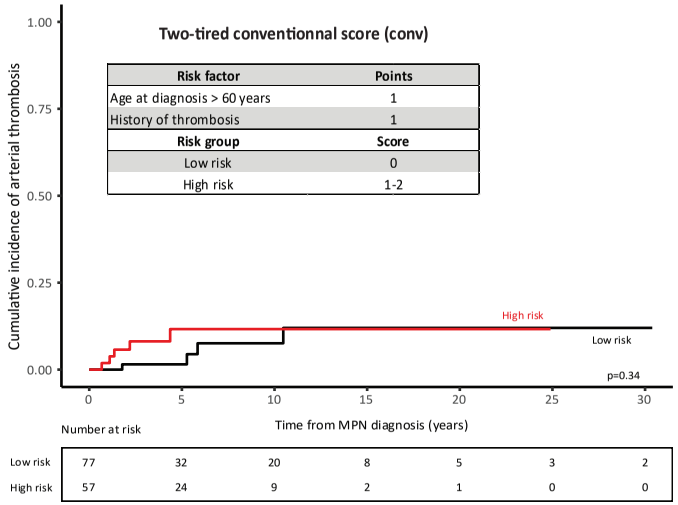
Figure S3



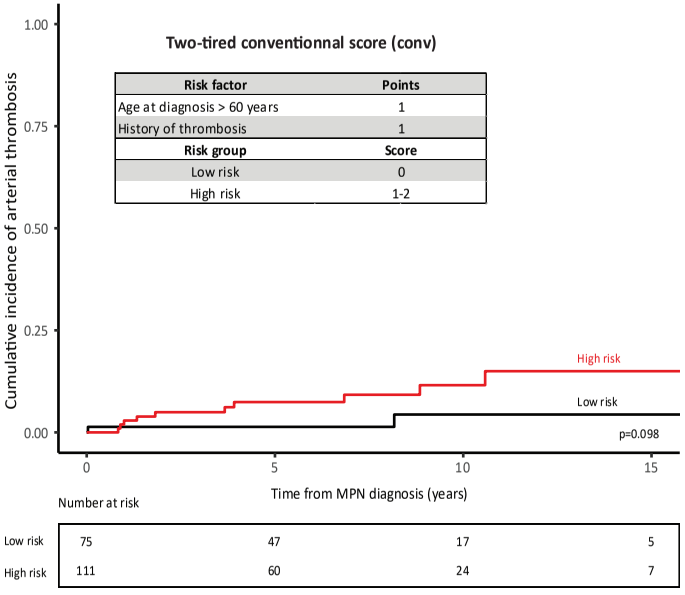
ARTS=0	344	257	173	111	64	38	17
ARTS=1	169	136	98	69	33	19	9
ARTS=2	55	31	13	7	1	1	1
ARTS=3	196	143	99	35	21	10	5
ARTS=4	99	80	52	24	16	9	1
ARTS=5	78	48	19	9	4	2	2
ARTS=6	85	47	18	6	2	1	0
ARTS=7	20	10	3	0	0	0	0

Figure S4

A. MPN Brest University Medical Center Cohort



B. ET Henri Mondor Cohort



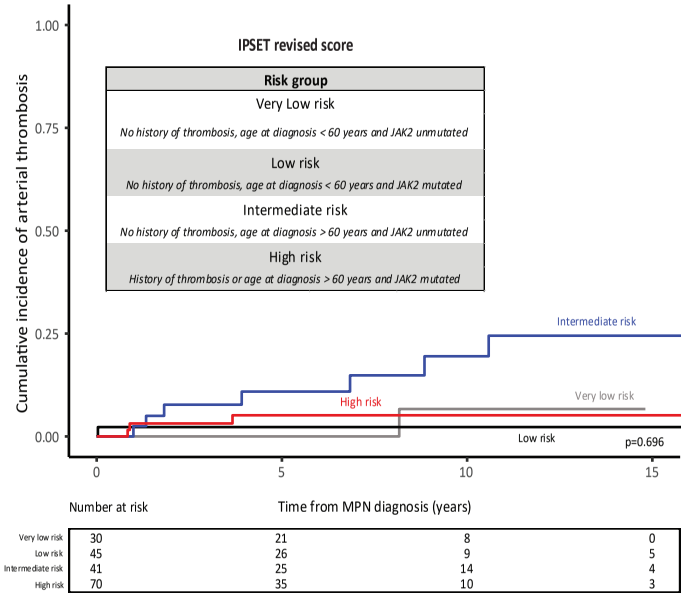
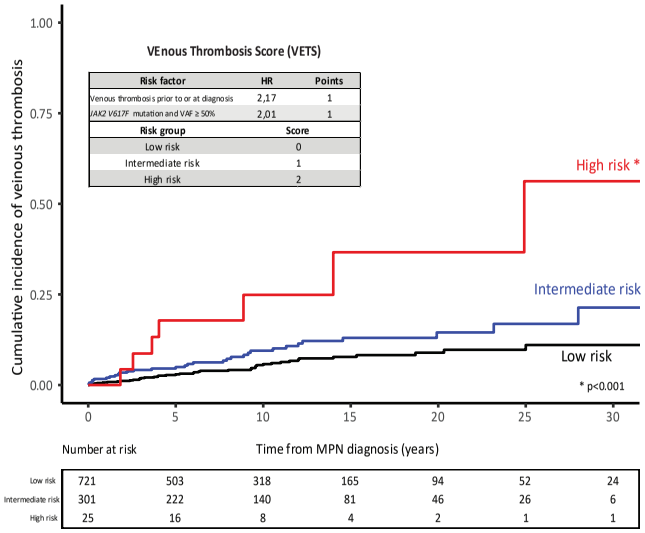


Figure S5

A.


VEnous Thrombosis Score (VETS)
Risk factor | HR | Points
Venous thrombosis prior to or at diagnosis | 2,17 | 1
JAK2 V617F mutation and VAF ≥ 50% | 2,01 | 1
Risk group | Score
Low risk | 0
Intermediate risk | 1
High risk | 2
Cumulative incidence of veinous thrombosis
1.00
0.75
0.50
0.25
0.00
High risk *
Intermediate risk
Low risk
* p<0.001
0
5
10
15
20
25
30
Number at risk
Time from MPN diagnosis (years)
Low risk 721 503 318 165 94 52 24
Intermediate risk 301 222 140 81 46 26 6
High risk 25 16 8 4 2 1 1

B.

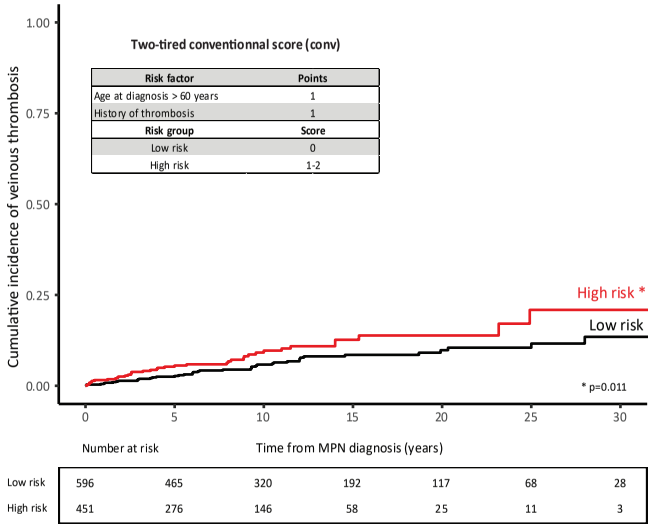

Two-tired conventionnal score (conv)
Risk factor | Points
Age at diagnosis > 60 years | 1
History of thrombosis | 1
Risk group | Score
Low risk | 0
High risk | 1-2
Cumulative incidence of veinous thrombosis
1.00
0.75
0.50
0.25
0.00
High risk *
Low risk
* p=0.011
0
5
10
15
20
25
30
Number at risk
Time from MPN diagnosis (years)
Low risk 596 465 320 192 117 68 28
High risk 451 276 146 58 25 11 3

Figure S6

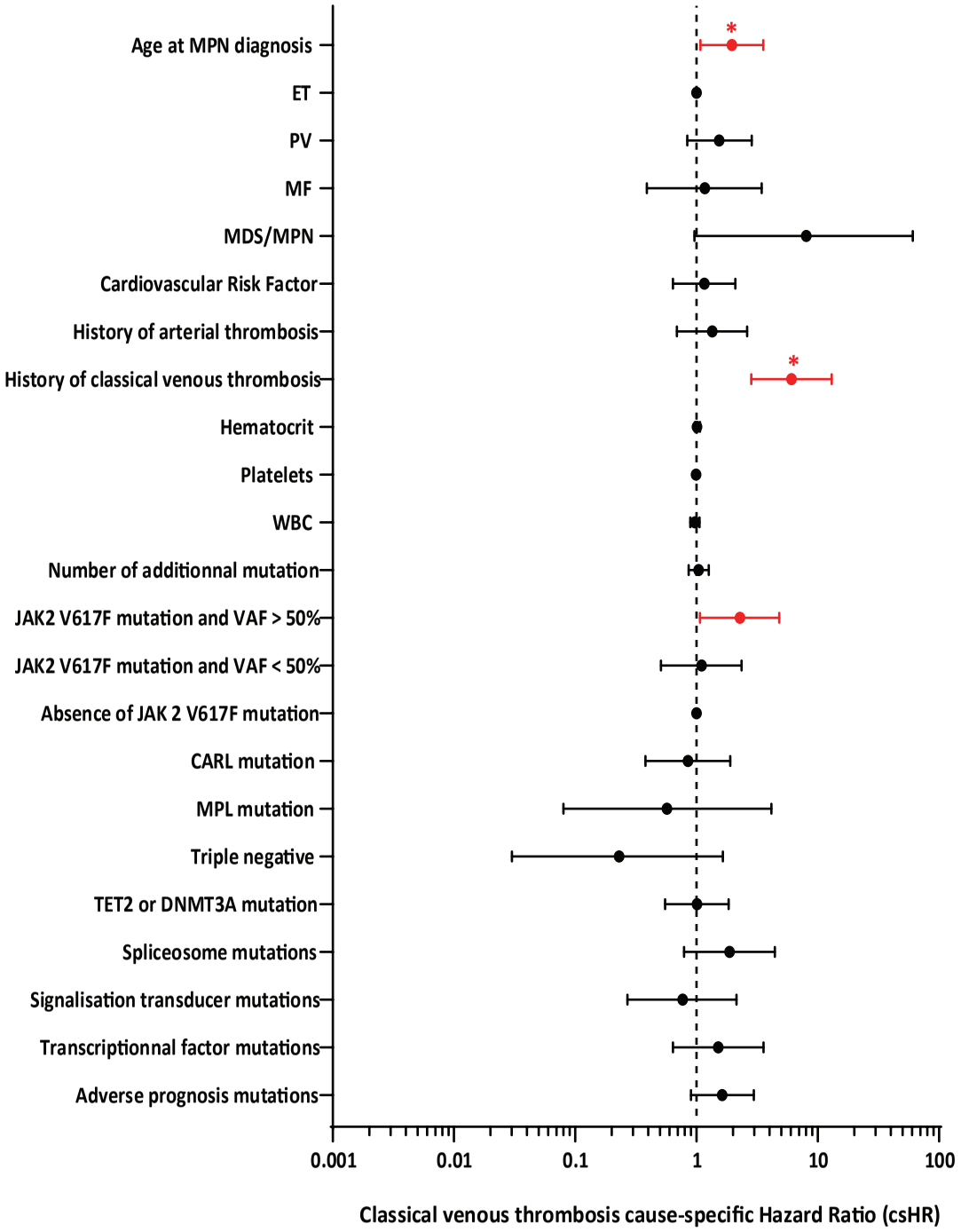

Age at MPN diagnosis
ET
PV
MF
MDS/MPN
Cardiovascular Risk Factor
History of arterial thrombosis
History of classical venous thrombosis
Hematocrit
Platelets
WBC
Number of additionnal mutation
JAK2 V617F mutation and VAF > 50%
JAK2 V617F mutation and VAF < 50%
Absence of JAK 2 V617F mutation
CARL mutation
MPL mutation
Triple negative
TET2 or DNMT3A mutation
Spliceosome mutations
Signalisation transducer mutations
Transcriptionnal factor mutations
Adverse prognosis mutations
*
*
0.001
0.01
0.1
1
10
100
Classical venous thrombosis cause-specific Hazard Ratio (csHR)

Figure S7

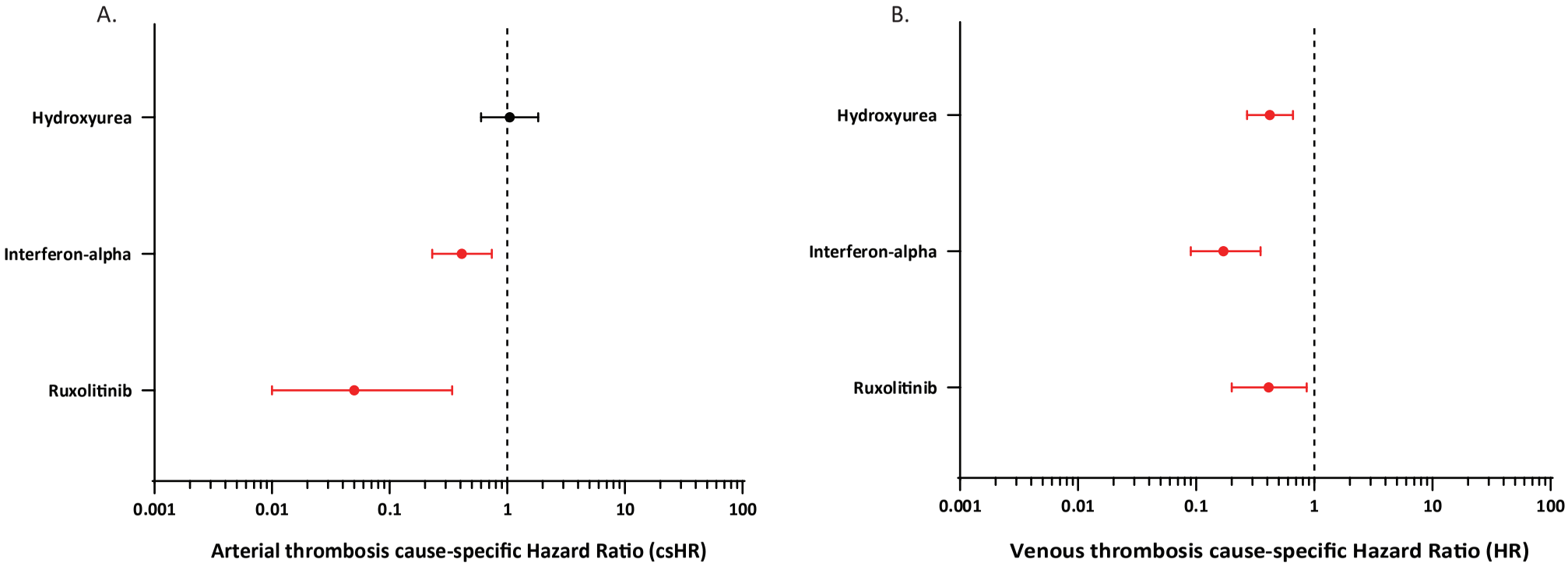
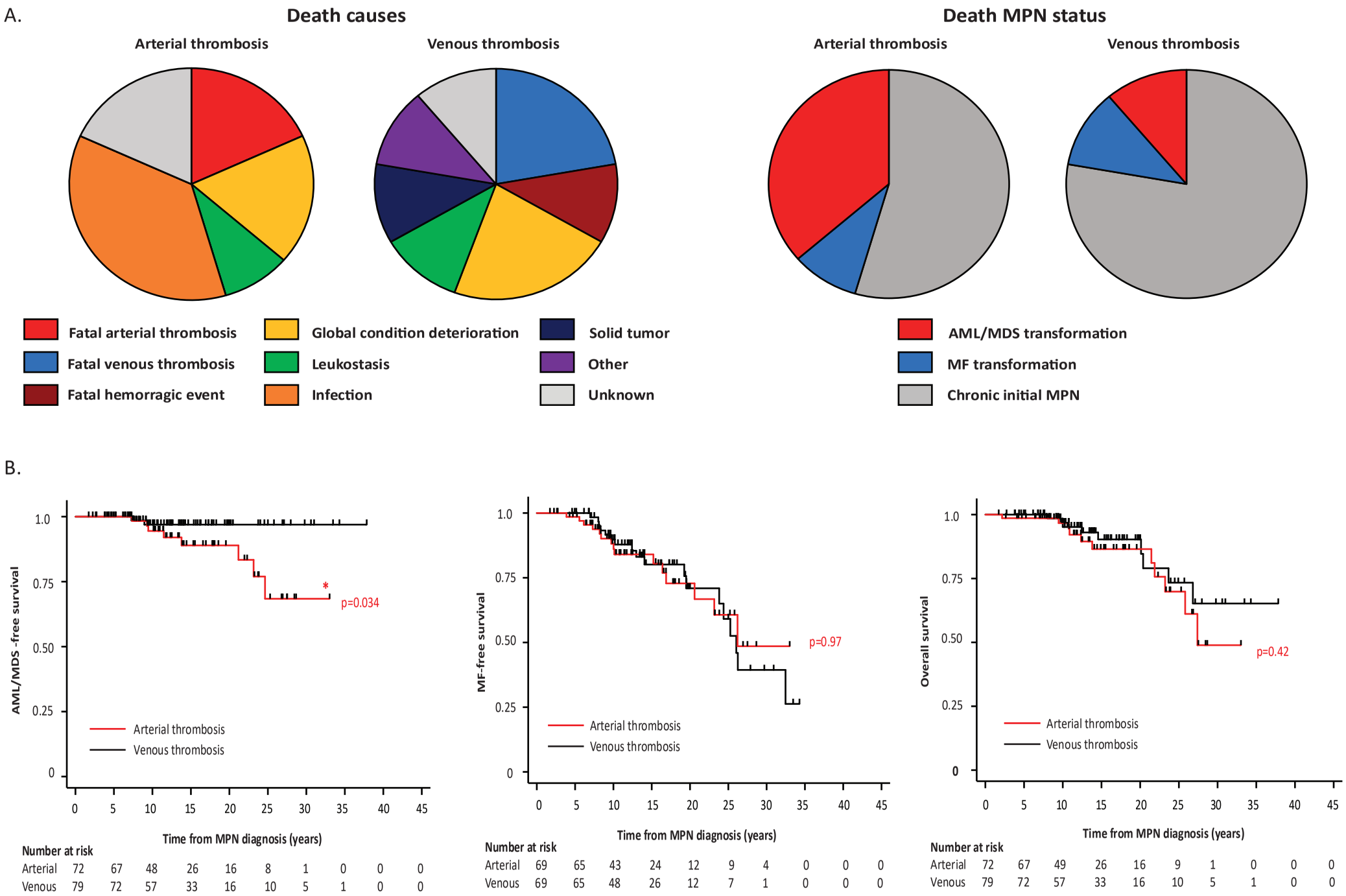

A.
Hydroxyurea
Interferon-alpha
Ruxolitinib
0.001
0.01
0.1
1
10
100
Arterial thrombosis cause-specific Hazard Ratio (csHR)
B.
Hydroxyurea
Interferon-alpha
Ruxolitinib
0.001
0.01
0.1
1
10
100
Venous thrombosis cause-specific Hazard Ratio (HR)

Figure S8


A.
Death causes
Arterial thrombosis
Venous thrombosis
Death MPN status
Arterial thrombosis
Venous thrombosis
Fatal arterial thrombosis
Fatal venous thrombosis
Fatal hemorragic event
Global condition deterioration
Leukostasis
Infection
Solid tumor
Other
Unknown
AML/MDS transformation
MF transformation
Chronic initial MPN
B.
AML/MDS -free survival
1.0
0.75
0.50
0.25
0
*
p=0.034
Arterial thrombosis
Venous thrombosis
0 5 10 15 20 25 30 35 40 45
Time from MPN diagnosis (years)
Number at risk
Arterial 72 67 48 26 16 8 1 0 0 0
Venous 79 72 57 33 16 10 5 1 0 0
MF-free survival
1.0
0.75
0.50
0.25
0
p=0.97
Arterial thrombosis
Venous thrombosis
0 5 10 15 20 25 30 35 40 45
Time from MPN diagnosis (years)
Number at risk
Arterial 69 65 43 24 12 9 4 0 0 0
Venous 69 65 48 26 12 7 1 0 0 0
Overall survival
1.0
0.75
0.50
0.25
0
p=0.42
Arterial thrombosis
Venous thrombosis
0 5 10 15 20 25 30 35 40 45
Time from MPN diagnosis (years)
Number at risk
Arterial 72 67 49 26 16 9 1 0 0 0
Venous 79 72 57 33 16 10 5 1 0 0