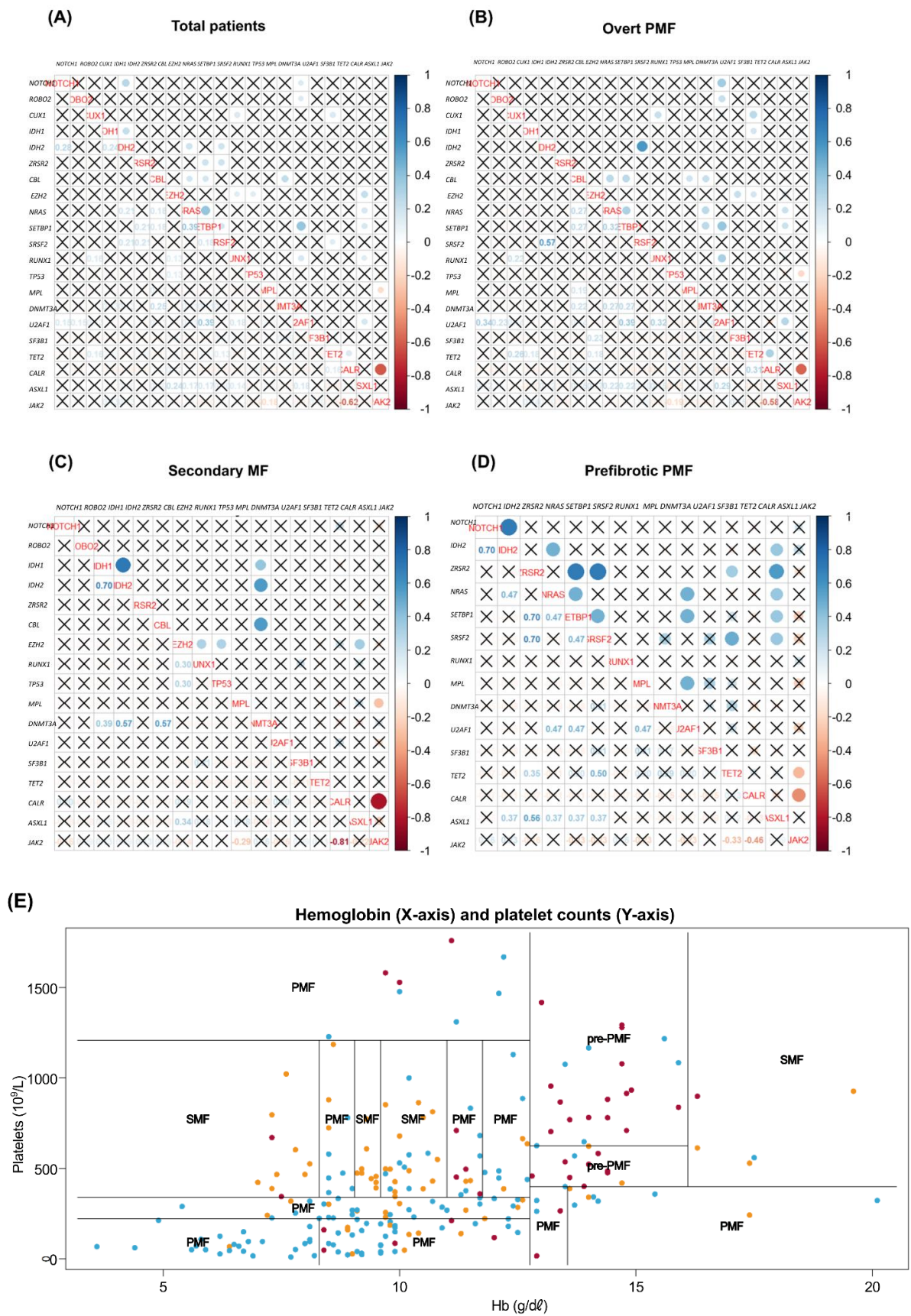
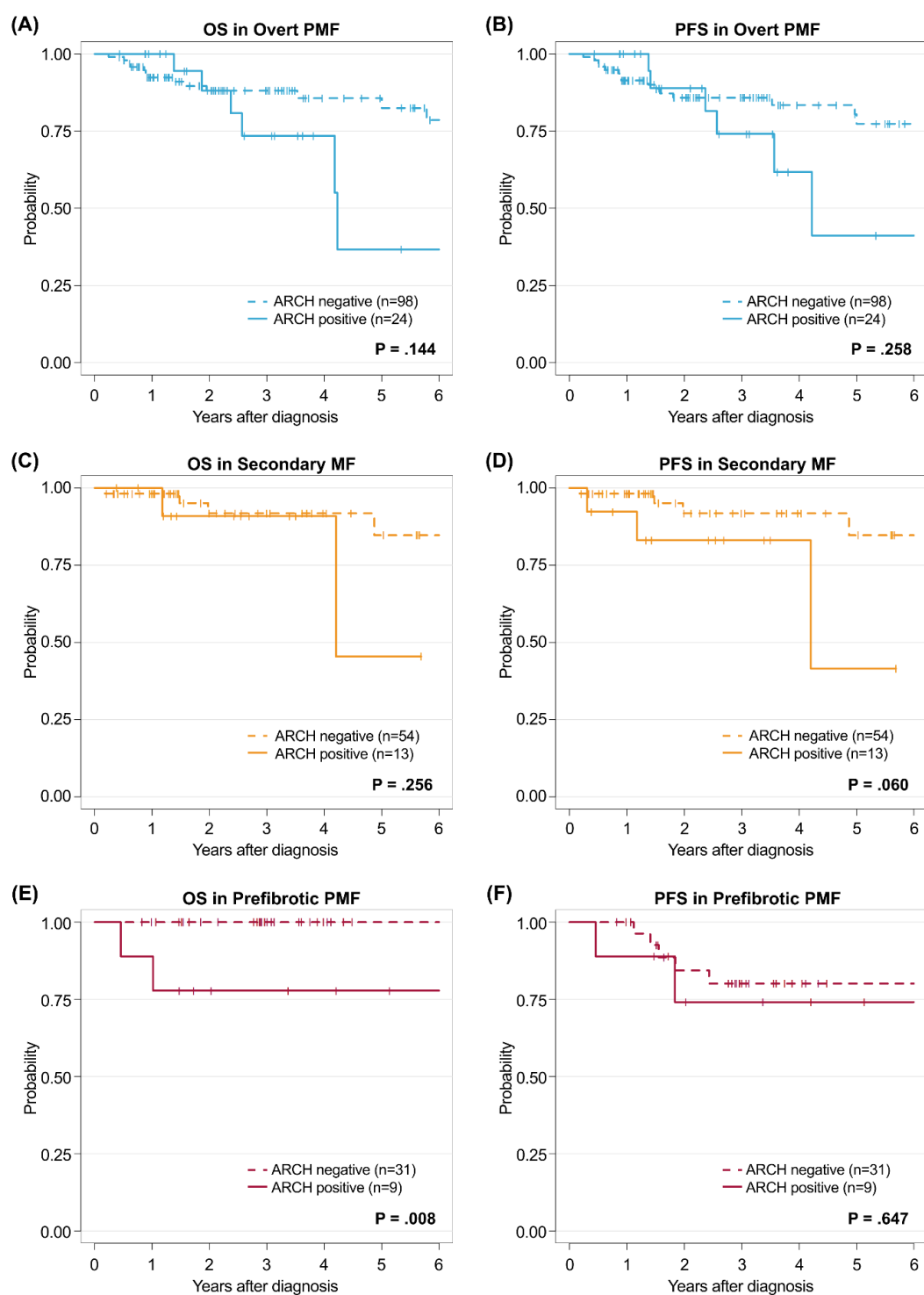


Supplementary Data



Supplementary Figure S1. Correlation between mutations in (A) overall cohort, (B) primary myelofibrosis (PMF), (C) secondary myelofibrosis (SMF), and (D) prefibrotic myelofibrosis (pre-PMF). X stands for p-value over 0.05; Numbers are correlation coefficient.

(E) Partition of PMF, SMF, and pre-PMF by the decision tree method according to hemoglobin level (X-axis) and platelet counts (Y-axis).



Supplementary Figure S2. Estimation of overall survival (OS) in (A) primary myelofibrosis (PMF), (C) secondary myelofibrosis (SMF), and (E) prefibrotic myelofibrosis (pre-PMF), and progression-free survival (PFS) in (B) PMF, (D) SMF, and (F) pre-PMF following CHIP of the high-risk progression group.

Supplementary Table S1. List of target genes in the NGS panel.

Target genes	Interval	Number of regions	Size (base pairs)
<i>ABCA12</i>	chr2:215797358-216002931	54	7929
<i>ABL1</i>	chr9:133589707-133761070	12	3529
<i>ASXL1</i>	chr20:30946579-31025141	17	4720
<i>ATM</i>	chr11:108098352-108236235	62	9171
<i>ATRX</i>	chrX:76763829-77041487	36	7543
<i>ATXN7L1</i>	chr7:105248299-105517004	15	3132
<i>BCOR</i>	chrX:39909169-39937182	15	5348
<i>BRAF</i>	chr7:140426294-140624503	21	2379
<i>BRCC3</i>	chrX:154299803-154348425	11	1021
<i>CALR</i>	chr19:13049494-13054795	10	1294
<i>CBL</i>	chr11:119077128-119170491	16	2721
<i>CBLB</i>	chr3:105377814-105588232	20	3079
<i>CD101</i>	chr1:117544440-117576723	9	3066
<i>CEBPA</i>	chr19:33792244-33793425	1	1182
<i>CREBBP</i>	chr16:3777719-3929917	31	7368
<i>CSF1R</i>	chr5:149433632-149465990	22	3003
<i>CSF3R</i>	chr1:36931697-36945097	16	2698
<i>CTCF</i>	chr16:67644736-67671775	10	2184
<i>CUX1</i>	chr7:101459311-101926382	34	5433
<i>DNMT1</i>	chr19:10244343-10311559	43	5292
<i>DNMT3A</i>	chr2:25457148-25536853	25	2888
<i>EGFR</i>	chr7:55086971-55273310	31	4084
<i>EP300</i>	chr22:41489009-41574960	31	7245
<i>ERG</i>	chr21:39739557-39947624	12	1764
<i>ETV6</i>	chr12:11803062-12044535	10	1443
<i>EZH2</i>	chr7:148504738-148544390	21	2456
<i>FBXW7</i>	chr4:153244033-153332955	14	2618
<i>FLT3</i>	chr13:28578189-28674647	25	3004
<i>GATA1</i>	chrX:48649517-48652675	5	1346
<i>GATA2</i>	chr3:128199862-128205874	5	1443
<i>GNAS</i>	chr20:57415162-57485884	17	4096
<i>HIPK2</i>	chr7:139257673-139477422	16	3708
<i>IDH1</i>	chr2:209101803-209116275	8	1248
<i>IDH2</i>	chr15:90627498-90645622	11	1359
<i>INVS</i>	chr9:102866804-103062956	17	3395
<i>IRF1</i>	chr5:131819643-131825170	9	978
<i>JAK2</i>	chr9:5021988-5126791	23	3399
<i>KDM2B</i>	chr12:121867919-122018816	29	4276
<i>KDM6A</i>	chrX:44732798-44970656	31	4470
<i>KIT</i>	chr4:55524182-55604723	21	2931
<i>KMT2A</i>	chr11:118307228-118392887	38	12082
<i>KMT2D</i>	chr12:49415563-49449107	55	16662
<i>KRAS</i>	chr12:25362729-25398318	6	708
<i>LAMB4</i>	chr7:107664484-107763609	35	5507
<i>MECOM</i>	chr3:168802697-169381160	20	3816
<i>MET</i>	chr7:116335811-116436178	21	4359
<i>MLL3</i>	chr7:151833917-152132871	62	15030
<i>MLL5</i>	chr7:104681400-104753780	27	5743
<i>MN1</i>	chr22:28146903-28196531	2	3963
<i>MPL</i>	chr1:43803520-43818443	12	1993
<i>NCOR2</i>	chr12:124809948-124979797	49	7734
<i>NF1</i>	chr17:29422226-29705949	63	9011
<i>NLRP1</i>	chr17:5405134-5487277	18	4493
<i>NOTCH1</i>	chr9:139390523-139440238	34	7668
<i>NPM1</i>	chr5:170814953-170837569	12	894

<i>NRAS</i>	chr1:115251156-115258781	4	570
<i>NRD1</i>	chr1:52254908-52344287	34	3696
<i>NUP98</i>	chr11:3692612-3803347	35	5567
<i>OCA2</i>	chr15:28000534-28327020	24	2573
<i>PDGFRA</i>	chr4:55106220-55161439	24	3450
<i>PHF12</i>	chr17:27233201-27278622	17	3519
<i>PHF6</i>	chrX:133511648-133559360	9	1207
<i>PRPF40B</i>	chr12:50017374-50037975	26	2682
<i>PRPF8</i>	chr17:1553953-1587865	42	7151
<i>PTPN11</i>	chr12:112856916-112942568	16	1822
<i>RAD21</i>	chr8:117859739-117878968	13	1896
<i>RAD50</i>	chr5:131893017-131978781	27	4211
<i>RINT1</i>	chr7:105172763-105207758	16	2417
<i>ROBO1</i>	chr3:78648063-79639061	34	5223
<i>ROBO2</i>	chr3:75986645-77695209	32	4862
<i>RUNX1</i>	chr21:36164432-36421196	11	1584
<i>RUNX1T1</i>	chr8:92972470-93115112	20	2350
<i>SETBP1</i>	chr18:42281312-42643663	6	4980
<i>SF3A1</i>	chr22:30730583-30752781	16	2382
<i>SF3B1</i>	chr2:198257027-198299723	27	4045
<i>SMC1A</i>	chrX:53407024-53449549	26	3882
<i>SMC3</i>	chr10:112327575-112364060	29	3654
<i>SRSF2</i>	chr17:74732243-74733242	2	666
<i>STAG2</i>	chrX:123156478-123234447	34	3861
<i>TET1</i>	chr10:70332096-70451571	11	6411
<i>TET2</i>	chr4:106111627-106197676	10	6165
<i>TP53</i>	chr17:7565257-7579912	14	1378
<i>TP53BP1</i>	chr15:43699581-43785241	31	6130
<i>U2AF1</i>	chr21:44513212-44527604	9	790
<i>U2AF2</i>	chr19:56166471-56185434	14	1541
<i>WT1</i>	chr11:32410604-32456891	11	1568
<i>ZRSR2</i>	chrX:15808619-15841365	12	1690

Supplementary Table S2. Genetic distribution of non-driver mutations in five subgroups by hierarchical clustering methods

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	P
	(n = 104)	(n = 44)	(n = 56)	(n = 11)	(n = 15)	
Myelofibrosis						.166
PMF, n (%)	53 (51.0)	25 (56.8)	35 (62.5)	4 (40.0)	5 (33.3)	
SMF, n (%)	28 (26.9)	11 (25.0)	18 (32.1)	3 (30.0)	7 (46.7)	
pre-PMF, n (%)	23 (22.1)	8 (18.2)	3 (5.4)	3 (30.0)	3 (20.0)	
<i>JAK2</i> , n (%)	56 (53.8)	21 (47.7)	28 (50.0)	8 (80.0)	7 (46.7)	.426
<i>CALR</i> _type, n (%)						.473

Type1/like	17 (16.3)	7 (15.9)	12 (21.4)	0 (0.0%)	3 (20.0)	
Type2/like	6 (5.8)	2 (4.5)	4 (7.1)	1 (10.0%)	3 (20.0)	
Others	2 (1.9)	0 (0.0)	2 (3.6)	0 (0.0%)	1 (6.7)	
<i>MPL</i> , n (%)	3 (2.9)	2 (4.5)	4 (7.1)	1 (10.0%)	0 (0.0)	.553
<i>ASXL1</i> , n (%)	0 (0.0)	11 (25.0)	55 (98.2)	0 (0.0%)	0 (0.0)	<.001
<i>CBL</i> , n (%)	0 (0.0)	5 (11.4)	0 (0.0)	0 (0.0%)	0 (0.0)	<.001
<i>CUX1</i> , n (%)	0 (0.0)	4 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	.002
<i>DNMT3A</i> , n (%)	0 (0.0)	11 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	<.001
<i>EZH2</i> , n (%)	0 (0.0)	0 (0.0)	5 (8.9)	0 (0.0)	0 (0.0)	.003
<i>IDH1</i> , n (%)	0 (0.0)	4 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	.002
<i>IDH2</i> , n (%)	0 (0.0)	2 (4.5)	2 (3.6)	0 (0.0)	0 (0.0)	.250
<i>NOTCH1</i> , n (%)	0 (0.0)	3 (6.8)	0 (0.0)	0 (0.0)	0 (0.0)	.012
<i>NRAS</i> , n (%)	0 (0.0)	2 (4.5)	3 (5.4)	0 (0.0)	0 (0.0)	.154
<i>RUNX1</i> , n (%)	0 (0.0)	6 (13.6)	2 (3.6)	0 (0.0)	0 (0.0)	.001
<i>SETBP1</i> , n (%)	0 (0.0)	3 (6.8)	2 (3.6)	0 (0.0)	0 (0.0)	.099
<i>SF3B1</i> , n (%)	0 (0.0)	2 (4.5)	5 (8.9)	10 (100.0)	0 (0.0)	<.001
<i>SRSF2</i> , n (%)	0 (0.0)	1 (2.3)	4 (7.1)	0 (0.0)	0 (0.0)	.053
<i>TET2</i> , n (%)	0 (0.0)	7 (15.9)	6 (10.7)	0 (0.0)	15 (100.0)	<.001
<i>TP53</i> , n (%)	0 (0.0)	7 (15.9)	1 (1.8)	0 (0.0)	0 (0.0)	<.001
<i>U2AF1</i> , n (%)	0 (0.0)	11 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	<.001
<i>ZRSR2</i> , n (%)	0 (0.0)	3 (6.8)	1 (1.8)	0 (0.0)	0 (0.0)	.064

SMF, secondary myelofibrosis; PMF, primary myelofibrosis; pre-PMF, prefibrotic,

myelofibrosis; n, number; P, p-value

Supplementary Table S3. *p*-value of OS and PFS in between clusters.

	C1 vs the other clusters	C2 vs the other clusters	C3 vs the other clusters	C1 vs C2	C1 vs C3	C2 vs. C3
Whole cohort						
OS, <i>p</i> -value	.035	.002	.386	.002	.079	.144
PFS, <i>p</i> -value	.033	.002	.421	.002	.088	.140
PMF						
OS, <i>p</i> -value	.188	.163	.468	.162	.226	.492
PFS, <i>p</i> -value	.097	.084	.677	.073	.224	.335
SMF						
OS, <i>p</i> -value	.239	.001	.411	.008	.946	.016
PFS, <i>p</i> -value	.157	.001	.872	.008	.449	.066
pre-PMF						
OS, <i>p</i> -value	.107	.317	.013	.114	.006	.522
PFS, <i>p</i> -value	.458	.522	.002	.468	.005	.152