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Supplementary information

Precision medicine treatment in acute myeloid leukemia using prospective genomic profiling: feasibility and preliminary efficacy of the Beat AML Master Trial

In the format provided by the authors and unedited

Supplementary Information

Statistics Supplemental Information

Per protocol, a one-sided Wald confidence interval was used to estimate the lower limit on the success rate to determine feasibility. With 109 patients, there was 90% power to rule out proportions of 0.8 or lower with 95% confidence. We therefore required 94/109 (86.2%) successes such that the 95% lower confidence bound on the estimate would be greater than 80%; 16/109 (14.7%) failures would have motivated early termination.

Supplementary Table 1. Reasons for Screen Fail of 92 patients from Figure 1B

Reason, no. (%)	Ineligible Patients (n=92)
Alternative Diagnosis	71 (77)
Confounding Medical Condition	6 (7)
Master Group A/B Criteria Not Met	5 (5)
Symptomatic CNS Involvement	3 (3)
Compliance Concerns	3 (3)
Leukostasis Requiring Urgent Therapy	1 (1)
Disseminated Intravascular Coagulopathy	1 (1)
Age Criteria Not Met	1 (1)
Viable Material Unavailable for Genetic Testing	1 (1)

Supplementary Table 2. Adverse Events of Special Interest for 26 patients

Adverse Events of Special Interest (AESI)	N
Death prior to treatment assignment due to AML progression	6
Life threatening bleeding (CNS, GI, acute hemorrhage requiring transfusion)	6
Progression of disease requiring therapy before treatment assignment	0
Worsening of performance status by more than 2 levels or new requirement for ICU care, intubation, or emergent surgery related to leukemia	8
Combination of Above AESI Categories*	6

*All 6 patients had life threatening bleeding, one with progression and death prior to treatment assignment, one with progression of disease requiring therapy before treatment assignment, three with worsening status related to leukemia, and one with worsening status related to AML progression and death prior to treatment assignment.

Supplementary Table 3. Treatment Options on Beat AML Master Trial

AML Subtype	Drug
CBF	Samalizumab (CD200 Ab) + induction
NPM1 + FLT3-ITD	Entospletinib (Syk inhibitor) + induction (fit) Entospletinib (Syk inhibitor) monotherapy (unfit)
MLL rearranged	Entospletinib (Syk inhibitor)
IDH2 +	Enasidenib
IDH1 +	Ivosidenib + Aza
TP53+	Entospletinib (Syk inhibitor) + Decitabine
TP53 - Complex Karotype (≥ 3 abn)	Entospletinib (Syk inhibitor) + Decitabine
TP53+	Pevonedistat (Nedd8 inhibitor) + Aza
FLT3-ITD+ or FLT3-TKD +	Gilteritinib monotherapy or + Decitabine
Tet2/WTI	BI 836858 (CD33 Ab) + Aza
Marker Negative	BI 836858 (CD33 Ab) + Aza

Supplementary Table 4. Distribution of patients in molecular groups defined by the prioritized schema and according to actual treatment assignment

Group, n (%)	Prioritized Schema (n = 395)	Treatment Assignment (n = 395)
CBF	9 (2.3)	2 (0.5)
NPM1+ FLT3-ITD WT	46 (11.7)	29 (7.3)
MLL Rearranged	11 (2.8)	7 (1.8)
IDH2+	45 (11.4)	54 (13.7)
IDH1+	23 (5.8)	11 (2.8)
TP53+	76 (19.2)	60 (15.2)
TP53 - Complex Karyotype (>3 abn)	31 (7.9)	15 (3.8)
FLT3-ITD+ or FLT3-TKD+	27 (6.8)	7 (1.8)
TET2 / WT1	49 (12.4)	64 (16.2)
Marker Negative	78 (19.8)	146 (37.0)

Supplementary Table 5. Treatment Assignments for All 395 Eligible Patients Screened for Beat AML

Prioritized Schema Group	Actual Treatment Assignment										
	CBF	NPM1	MLL	IDH2	IDH1	TP53	Complex	FLT3	TET2 / WT1	Marker-	Total
CBF	2	0	0	0	0	1	0	0	0	6	9 (2.3)
NPM1	0	26	0	9	2	0	0	0	4	5	46 (11.7)
MLL	0	0	7	1	0	0	0	0	1	2	11 (2.8)
IDH2	0	0	0	42	0	0	0	0	1	2	45 (11.4)
IDH1	0	1	0	0	9	0	0	0	10	3	23 (5.8)
TP53	0	0	0	0	0	58	0	0	0	18	76 (19.2)
Complex	0	0	0	0	0	0	15	0	4	12	31 (7.9)
FLT3	0	1	0	0	0	0	0	7	2	17	27 (6.8)
TET2 / WT1	0	1	0	0	0	0	0	0	42	6	49 (12.4)
Marker-	0	0	0	2	0	1	0	0	0	75	78 (19.8)
Total	2 (0.5)	29 (7.3)	7 (1.8)	54 (13.7)	11 (2.8)	60 (15.2)	15 (3.8)	7 (1.8)	64 (16.2)	146 (37.0)	395 (100)

Supplementary Table 6. Treatment Assignments for All 224 Eligible Patients Treated on a Beat AML Sub-study

Prioritized Schema Group	Actual Treatment Assignment										
	CBF	NPM1	MLL	IDH2	IDH1	TP53	Complex	FLT3	TET2 / WT1	Marker-	Total
CBF	2	0	0	0	0	1	0	0	0	2	5 (2.2)
NPM1	0	15	0	8	2	0	0	0	2	3	30 (13.4)
MLL	0	0	1	1	0	0	0	0	1	1	4 (1.8)
IDH2	0	0	0	28	0	0	0	0	0	1	29 (13.0)
IDH1	0	1	0	0	5	0	0	0	4	0	10 (4.5)
TP53	0	0	0	0	0	37	0	0	0	5	42 (18.8)
Complex	0	0	0	0	0	0	7	0	3	7	17 (7.6)
FLT3	0	1	0	0	0	0	0	4	0	10	15 (6.7)
TET2 / WT1	0	1	0	0	0	0	0	0	22	3	26 (11.6)
Marker-	0	0	0	2	0	0	0	0	0	44	46 (20.5)
Total	2 (0.9)	18 (8.0)	1 (0.5)	39 (17.4)	7 (3.1)	38 (17.0)	7 (3.1)	4 (1.8)	32 (14.3)	76 (33.9)	224 (100)

Supplementary Table 7. Percentage of eligible Beat AML Patients with mutations in common genes

Gene	Percentage (%)
TP53	26
DNMT3A	24
IDH2	22.5
SRSF2	22.5
ASXL1	22.5
RUNX1	20.6
NPM1	20.1
NRAS	18.1
TET2	17.2
FLT3	15.7
PTPN11	14.2
STAG2	12.7
CEBPA	8.8
IDH1	7.8
SF3B1	7.4
BCOR	6.9
U2AF1	6.9
KRAS	6.9
NF1	6.4
JAK2	5.4
EZH2	3.4
GATA2	3.4
PHF6	3.4
CBL	2.9
WT1	2.9
BCORL1	2.9
SETBP1	2.5
MUTYH	2
MLL2	2
CHEK2	2

Supplementary Table 8. Most commonly mutated genes across the different Beat AML groups compared to previous studies

Gene	Papaemmanuil et al.	AML TCGA	Beat AML/ Oregon	Beat AML Consented Patients	Beat AML Eligible Patients	Beat AML Patients Treated on Sub-study	Beat AML Consented Patients with VAF>30	Beat AML Eligible Patients with VAF>30	Beat AML Patients Treated on Sub-study with VAF>30
TP53	7.15	8	8.7	26.69	26.45	26.34	17.86	19.14	18.30
DNMT3A	25.64	24.5	22.3	25.87	27.96	28.57	20.53	22.67	22.77
ASXL1	5.03	2.5	7.9	23.82	23.43	24.11	19.51	19.14	19.64
TET2	11.05	8.5	12.2	23.00	23.17	21.88	19.51	19.65	18.75
RUNX1	9.7	13	12.5	21.56	22.92	25.45	14.78	15.62	15.63
SRSF2	6.59	NA	11.4	21.15	21.91	24.11	17.66	18.39	20.54
NRAS	19.12	7.5	12.4	18.48	18.64	17.86	6.16	6.30	4.46
FLT3	36.47	28	28.8	16.84	18.39	17.41	4.52	4.28	5.36
NPM1	31.16	27	21.7	16.63	19.14	19.64	11.50	13.60	14.29
IDH2	10.69	10	11.9	16.02	18.64	22.77	11.91	14.11	17.41
MLL	5.59	NA	NA	12.53	13.60	14.29	4.11	4.53	5.80
PTPN11	8.5	4.5	4.7	10.68	11.34	13.84	3.49	4.03	4.91
STAG2	4.75	3	5.3	10.27	11.08	12.95	5.95	6.05	7.14
IDH1	7.51	9.5	8.7	10.06	11.08	8.48	6.98	7.81	7.14
BCOR	2.55	NA	5.5	9.65	9.57	8.93	7.39	7.05	7.14
KRAS	5.59	4	4	9.03	8.82	6.70	1.85	2.02	1.34
U2AF1	2.62	4	4.7	8.83	8.56	6.70	5.75	6.05	3.57
JAK2	0.78	NA	4.5	8.42	7.30	6.25	4.72	4.03	3.57
CEBPA	9.77	6.5	5.3	7.80	8.82	9.38	4.93	5.54	5.36

EZH2	3.26	1.5	3.5	6.57	6.05	5.80	5.34	4.79	5.36
GATA2	2.62	1	4	6.37	6.55	8.48	3.08	3.02	3.57
SF3B1	2.83	NA	5.1	6.37	5.79	7.59	3.90	3.53	4.91
KMT2A	NA	5	NA	3.90	4.53	3.57	0.00	0.00	0.00
WT1	5.45	6	9	3.90	3.78	4.02	2.87	2.52	3.13
KIT	4.67	4	1.8	2.67	3.27	4.46	2.26	2.77	4.02
RAD21	3.82	2	2.6	2.26	2.02	1.34	1.03	1.26	1.34
RUNX1T1	NA	4	NA	2.26	1.76	1.79	1.44	1.26	1.34
MYH11	NA	5	NA	1.64	1.76	1.79	0.00	0.00	0.00
RARA	NA	8	NA	1.23	1.26	0.89	0.82	1.01	0.45
CBFB	NA	6	NA	0.00	0.00	0.00	0.00	0.00	0.00
PML	NA	8	NA	0.00	0.00	0.00	0.00	0.00	0.00

Supplementary Table 9. Multivariable models for overall survival that controlled for demographic, clinical and molecular variables. Modeling was performed on a dataset with 395 patients and 194 events. Multiple imputation estimated missing data. Log hazards and standard errors for each variable were estimated using Cox proportional hazards models for each of 10 imputed datasets. Estimates of log hazards and standard errors were combined across the imputed datasets. Hazard ratios with 95% confidence intervals were obtained from the log hazards and standard errors. P-values from two-sided t-tests are provided. P-values were not adjusted for multiple testing.

Variable	Univariable Models			Full Multivariable Model		
	Hazard Ratio	95% CI	P	Hazard Ratio	95% CI	P
Standard vs Beat AML Therapy						
Before 3 months	3.33	2.12-5.24	<.0001	2.86	1.77-4.61	<.0001
After 3 months	1.27	0.73-2.20	0.3970	1.13	0.63-2.03	0.6747
Investigational vs Beat AML Therapy	0.68	0.36-1.26	0.2202	0.65	0.33-1.31	0.2283
Palliative Care vs Beat AML Therapy						
Before 1 month	28.70	15.66-52.58	<.0001	26.67	13.77-51.67	<.0001
After 1 month	2.32	1.08-5.02	0.0320	2.30	0.98-5.40	0.0556
Age (5-year increase)	1.27	1.14-1.41	<.0001	1.22	1.09-1.37	0.0007
Female vs Male	0.78	0.58-1.04	0.0844	0.85	0.6-1.21	0.3618
Non-white vs White	0.73	0.43-1.23	0.2326	0.86	0.48-1.54	0.6065
ECOG PS 2+ vs 0/1	2.27	1.68-3.07	<.0001	1.89	1.34-2.65	0.0003
Hemoglobin (1-unit increase)	0.89	0.81-0.98	0.0173	0.96	0.86-1.07	0.4470
Platelet (50-unit increase)	0.94	0.86-1.03	0.1762	0.98	0.89-1.08	0.7190
WBC (50-unit increase)	1.27	1.05-1.54	0.0153	1.28	0.97-1.69	0.0816
%Blood Blasts (10-unit increase)	1.04	0.99-1.09	0.1051	0.98	0.91-1.06	0.6430
%Bone Marrow Blasts (10-unit increase)	1.07	1.01-1.14	0.0245	1.14	1.05-1.24	0.0017
Alanine Aminotransferase (10-unit increase)	1.04	0.97-1.11	0.3016	1.03	0.9-1.17	0.6895
Aspartate Aminotransferase (10-unit increase)	1.06	1.01-1.11	0.0310	0.97	0.86-1.10	0.6413
Total Bilirubin (0.2-unit increase)	1.05	1.02-1.08	0.0011	1.05	1.01-1.09	0.0157
Creatinine (0.2-unit increase)	1.11	1.04-1.19	0.0022	1.08	0.99-1.17	0.0882
Treatment-related AML: Yes vs No	1.34	0.94-1.92	0.1092	1.31	0.87-1.97	0.1960
CBF: Present vs Absent	0.28	0.04-1.82	0.1846	0.23	0.03-1.61	0.1401

MLL: Present vs Absent	2.80	1.36-5.74	0.0053	2.17	0.95-4.96	0.0674
Complex Karyotype: Present vs Absent	2.25	1.68-3.01	<.0001	1.26	0.8-1.98	0.3272
NPM1: Mutated vs Wild-type	0.78	0.53-1.15	0.2132	0.56	0.34-0.94	0.0277
IDH2: Mutated vs Wild-type	0.60	0.39-0.91	0.0173	0.79	0.47-1.34	0.3887
IDH1: Mutated vs Wild-type	0.75	0.44-1.27	0.2790	1.18	0.62-2.26	0.6173
TP53: Mutated vs Wild-type	2.11	1.54-2.89	<.0001	2.47	1.51-4.04	0.0004
FLT3 ITD: Present vs Absent	1.59	1.04-2.44	0.0342	1.36	0.82-2.28	0.2384
FLT3 TKD: Mutated vs Wild-type	1.10	0.49-2.49	0.8151	1.54	0.61-3.9	0.3646
FLT3 Other: Mutated vs Wild-type	1.78	0.57-5.58	0.3214	0.91	0.25-3.34	0.8875
TET2: Mutated vs Wild-type	1.21	0.87-1.68	0.2635	1.39	0.94-2.07	0.1021
WT1: Mutated vs Wild-type	1.29	0.61-2.75	0.5063	2.12	0.94-4.77	0.0702

Supplementary Table 10. Models for overall survival including all eligible patients without adverse events of special interest. Modeling was performed on a dataset with 369 patients and 174 events. Multiple imputation estimated missing data. Log hazards and standard errors for each variable were estimated using Cox proportional hazards models for each of 10 imputed datasets. Estimates of log hazards and standard errors were combined across the imputed datasets. Hazard ratios with 95% confidence intervals were obtained from the log hazards and standard errors. P-values from two-sided t-tests are provided. P-values were not adjusted for multiple testing.

Variable	Univariable Models			Full Multivariable Model		
	Hazard Ratio	95% CI	P	Hazard Ratio	95% CI	P
Standard vs Beat AML Therapy						
Before 3 months	2.90	1.78-4.73	<.0001	2.48	1.47-4.19	0.0008
After 3 months	1.06	0.58-1.92	0.8539	0.92	0.49-1.74	0.7957
Investigational vs Beat AML Therapy	0.67	0.36-1.26	0.2148	0.67	0.33-1.33	0.2511
Palliative Care vs Beat AML Therapy						
Before 1 month	27.78	13.96-55.27	<.0001	25.14	11.74-53.85	<.0001
After 1 month	2.77	1.28-5.98	0.0096	2.93	1.24-6.94	0.0149
Age (5-year increase)	1.28	1.15-1.43	<.0001	1.25	1.10-1.41	0.0004
Female vs Male	0.76	0.56-1.03	0.0776	0.83	0.58-1.20	0.3300
Non-white vs White	0.75	0.43-1.29	0.2966	0.97	0.52-1.78	0.9156
ECOG PS 2+ vs 0/1	2.33	1.69-3.22	<.0001	2.13	1.49-3.03	<.0001
Hemoglobin (1-unit increase)	0.91	0.82-1.00	0.0523	0.98	0.87-1.10	0.7015
Platelet (50-unit increase)	0.95	0.86-1.04	0.2582	0.98	0.89-1.08	0.6480
WBC (50-unit increase)	1.21	0.97-1.50	0.0882	1.2	0.89-1.62	0.2386
%Blood Blasts (10-unit increase)	1.05	1.00-1.11	0.0457	1.02	0.94-1.11	0.6312
%Bone Marrow Blasts (10-unit increase)	1.05	0.98-1.12	0.1425	1.11	1.01-1.21	0.0291
Alanine Aminotransferase (10-unit increase)	1.00	0.92-1.09	0.9638	1.02	0.88-1.18	0.8140
Aspartate Aminotransferase (10-unit increase)	1.04	0.97-1.10	0.2722	0.97	0.85-1.10	0.6041
Total Bilirubin (0.2-unit increase)	1.04	1.00-1.08	0.0327	1.05	1.00-1.10	0.0544
Creatinine (0.2-unit increase)	1.08	1.00-1.17	0.0532	1.04	0.94-1.15	0.4498
Treatment-related AML: Yes vs No	1.37	0.94-1.99	0.1042	1.36	0.89-2.09	0.1588
CBF: Present vs Absent	0.27	0.04-1.93	0.1945	0.21	0.03-1.69	0.1459

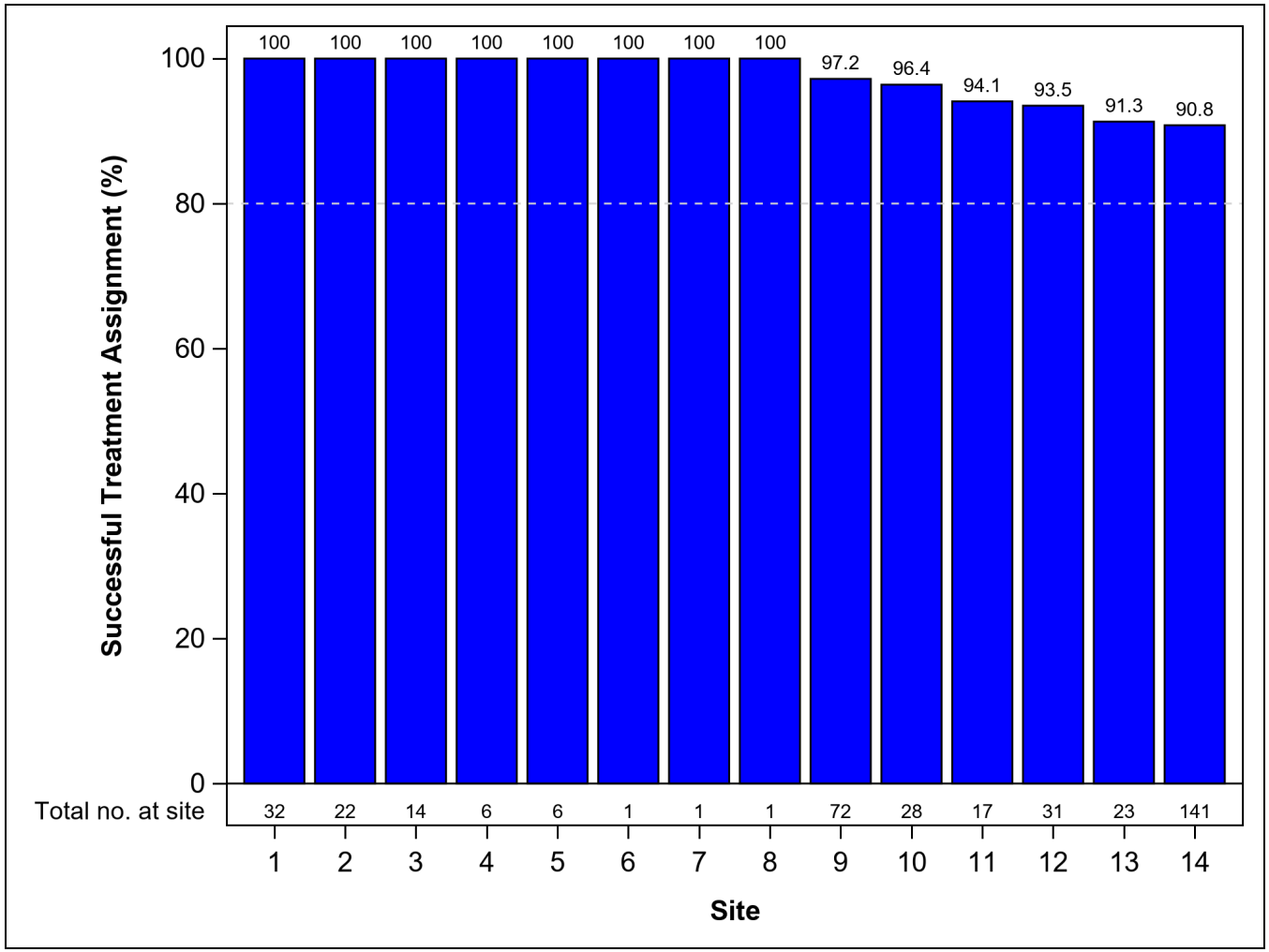
MLL: Present vs Absent	2.43	1.06-5.55	0.0365	2.05	0.81-5.18	0.1314
Complex Karyotype: Present vs Absent	2.30	1.69-3.13	<.0001	1.35	0.84-2.19	0.2198
NPM1: Mutated vs Wild-type	0.69	0.45-1.07	0.0956	0.53	0.3-0.92	0.0255
IDH2: Mutated vs Wild-type	0.61	0.39-0.94	0.0266	0.79	0.46-1.36	0.3864
IDH1: Mutated vs Wild-type	0.77	0.44-1.33	0.3422	1.18	0.6-2.29	0.6322
TP53: Mutated vs Wild-type	2.17	1.56-3.02	<.0001	2.21	1.31-3.71	0.0031
FLT3 ITD: Present vs Absent	1.65	1.05-2.58	0.0284	1.48	0.86-2.55	0.1605
FLT3 TKD: Mutated vs Wild-type	0.86	0.32-2.32	0.7678	1.49	0.47-4.72	0.5006
FLT3 Other: Mutated vs Wild-type	2.04	0.65-6.41	0.2205	1.31	0.34-5.00	0.6908
TET2: Mutated vs Wild-type	1.16	0.82-1.66	0.4042	1.36	0.89-2.08	0.1575
WT1: Mutated vs Wild-type	1.44	0.67-3.07	0.3484	2.28	1.01-5.17	0.0485

Supplementary Table 11. Models for overall survival including all eligible patients, landmarked at 15 days. Modeling was performed on a dataset with 315 patients and 166 events. Multiple imputation estimated missing data. Log hazards and standard errors for each variable were estimated using Cox proportional hazards models for each of 10 imputed datasets. Estimates of log hazards and standard errors were combined across the imputed datasets. Hazard ratios with 95% confidence intervals were obtained from the log hazards and standard errors. P-values from two-sided t-tests are provided. P-values were not adjusted for multiple testing.

Variable	Univariable Models			Full Multivariable Model		
	Hazard Ratio	95% CI	P	Hazard Ratio	95% CI	P
Standard vs Beat AML Therapy						
Before 3 months	2.97	1.85-4.78	<.0001	2.57	1.55-4.26	0.0003
After 3 months	1.28	0.74-2.22	0.3823	1.14	0.63-2.07	0.6589
Investigational vs Beat AML Therapy	0.67	0.36-1.26	0.2148	0.66	0.33-1.33	0.2445
Palliative Care vs Beat AML Therapy						
Before 1 month	14.65	6.59-32.55	<.0001	13.59	5.63-32.84	<.0001
After 1 month	2.29	1.06-4.96	0.0353	2.07	0.86-4.99	0.1060
Age (5-year increase)	1.25	1.12-1.40	<.0001	1.24	1.09-1.4	0.0008
Female vs Male	0.78	0.57-1.07	0.1253	0.80	0.54-1.19	0.2770
Non-white vs White	0.86	0.50-1.46	0.5672	1.08	0.59-2	0.8016
ECOG PS 2+ vs 0/1	2.27	1.64-3.14	<.0001	2.21	1.52-3.21	<.0001
Hemoglobin (1-unit increase)	0.92	0.84-1.02	0.1236	1.01	0.9-1.13	0.8952
Platelet (50-unit increase)	0.95	0.87-1.04	0.2863	0.97	0.88-1.07	0.5368
WBC (50-unit increase)	1.16	0.92-1.46	0.2105	1.06	0.77-1.46	0.7385
%Blood Blasts (10-unit increase)	1.05	1.00-1.10	0.0769	1.02	0.94-1.11	0.6757
%Bone Marrow Blasts (10-unit increase)	1.07	1.00-1.14	0.0558	1.14	1.04-1.25	0.0081
Alanine Aminotransferase (10-unit increase)	1.01	0.93-1.09	0.8051	1.03	0.89-1.18	0.7216
Aspartate Aminotransferase (10-unit increase)	1.03	0.96-1.10	0.3870	0.95	0.83-1.09	0.4838
Total Bilirubin (0.2-unit increase)	1.04	1.00-1.08	0.0453	1.05	1.00-1.10	0.0607
Creatinine (0.2-unit increase)	1.07	0.99-1.16	0.0940	1.03	0.93-1.14	0.5999
Treatment-related AML: Yes vs No	1.40	0.95-2.05	0.0860	1.38	0.90-2.12	0.1367
CBF: Present vs Absent	0.31	0.05-2.02	0.2240	0.25	0.03-1.84	0.1757

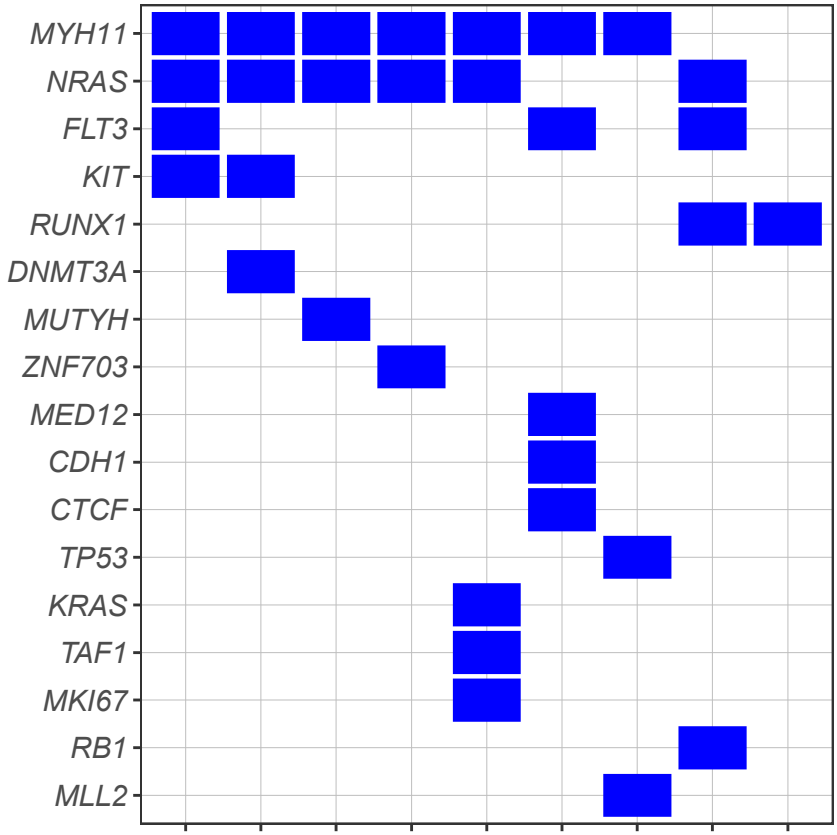
MLL: Present vs Absent	2.35	0.97-5.69	0.0596	1.71	0.63-4.62	0.291
Complex Karyotype: Present vs Absent	2.09	1.52-2.88	<.0001	1.33	0.82-2.17	0.2523
NPM1: Mutated vs Wild-type	0.74	0.49-1.12	0.1571	0.63	0.36-1.08	0.0944
IDH2: Mutated vs Wild-type	0.66	0.43-1.00	0.0521	0.72	0.41-1.24	0.2358
IDH1: Mutated vs Wild-type	0.73	0.42-1.29	0.2847	1.14	0.56-2.30	0.7240
TP53: Mutated vs Wild-type	1.87	1.32-2.67	0.0005	2.08	1.22-3.57	0.0080
FLT3 ITD: Present vs Absent	1.61	1.02-2.55	0.0417	1.38	0.8-2.39	0.2526
FLT3 TKD: Mutated vs Wild-type	1.01	0.42-2.47	0.9792	1.60	0.58-4.44	0.3651
FLT3 Other: Mutated vs Wild-type	1.42	0.35-5.72	0.6251	1.26	0.23-6.86	0.7893
TET2: Mutated vs Wild-type	1.15	0.8-1.64	0.4548	1.30	0.84-2.01	0.2331
WT1: Mutated vs Wild-type	1.72	0.81-3.68	0.1596	2.42	1.06-5.50	0.0360

Supplementary Figure 1: Treatment assignment success rates by site with a reference line at 80% (the null unacceptable rate).



Supplementary Figure 2. Co-mutation plots for patients enrolled in the trial under different molecular groups. Each column represents an individual patient and each blue box indicates a genomic alteration is present at any VAF detected. Genes in with genomic alterations are listed in descending order of frequency and each column represents an individual patient. **A)** Co-mutation plot for all patients enrolled in the trial in the CBF molecular group (n= 9). **B)** Co-mutation plot for all patients enrolled in the trial in the NPM1 molecular group (n=46). **C)** Co-mutation plot for all patients enrolled in the trial in the MLL molecular group (n=11). **D)** Co-mutation plot for all patients enrolled in the trial in the IDH2 molecular group (n= 45). **E)** Co-mutation plot for all patients enrolled in the trial in the IDH1 molecular group (n= 23). **F)** Co-mutation plot for all patients enrolled in the trial in the TP53 molecular group (n=76). **G)** Co-mutation plot for all patients enrolled in the trial in the complex karyotype group (n= 31). **H)** Co-mutation plot for all patients enrolled in the trial in the FLT3 molecular group (n= 27). **I)** Co-mutation plot for all patients enrolled in the trial in the TET2/WT1 molecular group (n=49). **J)** Co-mutation plot for all patients enrolled in the trial in the Marker negative molecular group (n= 78).

A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ZNF703
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CDH1
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TP53
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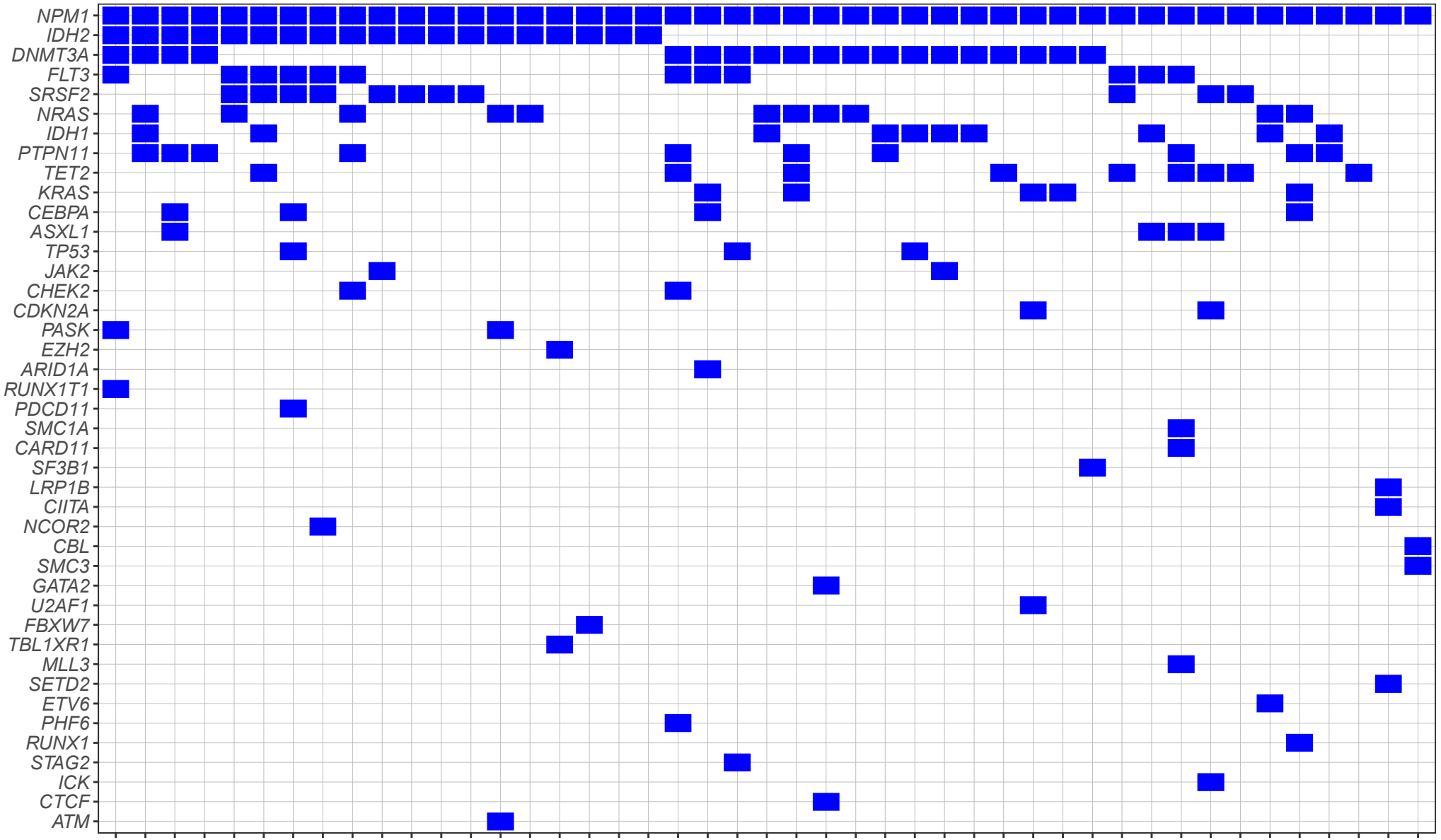
MKI67
RB1
MLL2

B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JAK2
CHEK2
CDKN2A
PASK
EZH2
ARID1A
RUNX1T1
PDCD11
SMC1A
CARD11
SF3B1
LRP1B
CIITA
NCOR2
CBL
SMC3
GATA2
U2AF1
FBXW7
TBL1XR1
MLL3
SETD2
ETV6
PHF6
RUNX1
STAG2
ICK
CTCF
ATM

C


MLL
KRAS
U2AF1
CBL
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KMT2A
NRAS
MLLT10
RUNX1
MLL3
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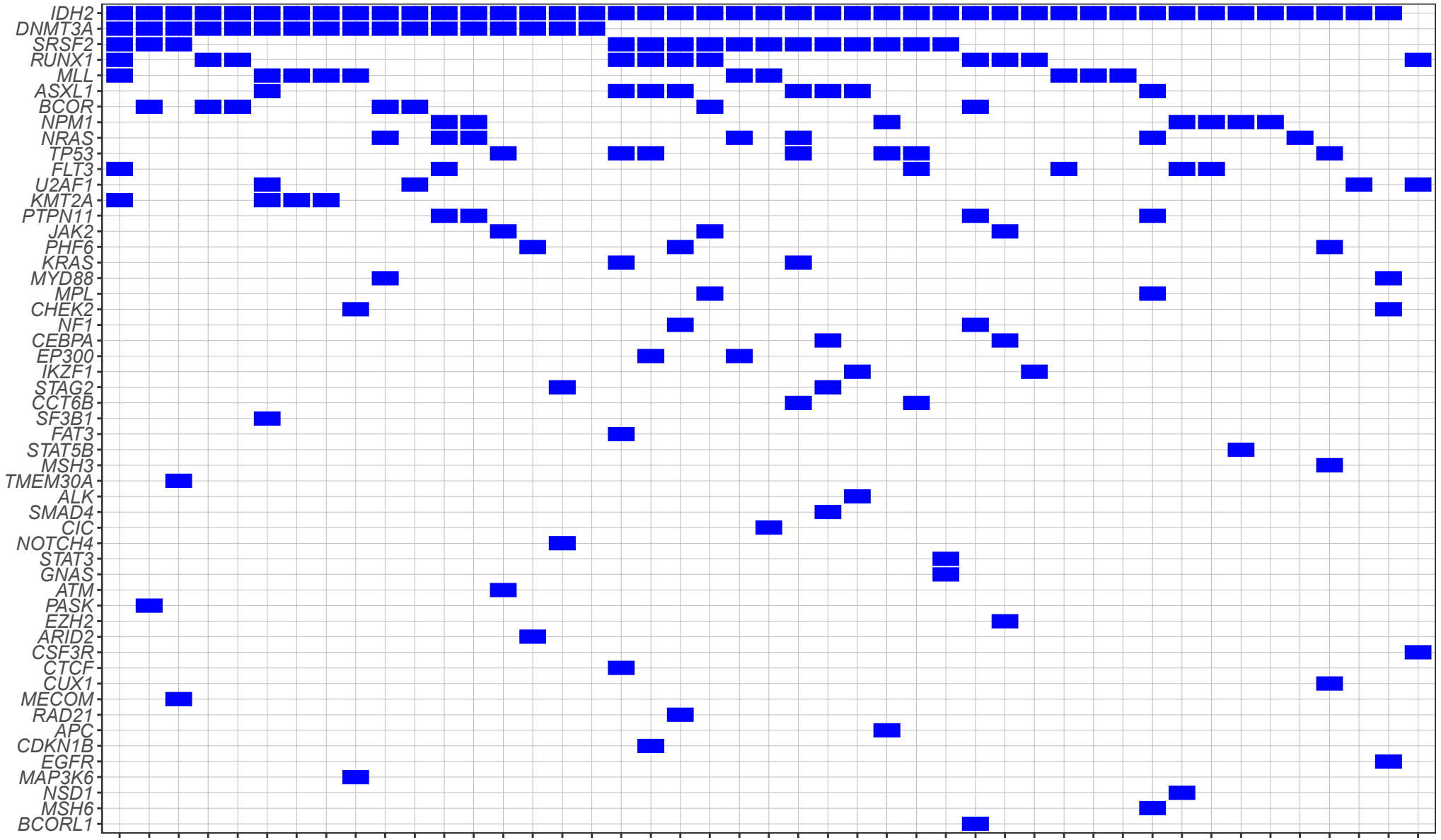
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JAK2
PHF6
KRAS
MYD88
MPL
CHEK2
NF1
CEBPA
EP300
IKZF1
STAG2
CCT6B
SF3B1
FAT3
STAT5B
MSH3
TMEM30A
ALK
SMAD4
CIC
NOTCH4
STAT3
GNAS
ATM
PASK
EZH2
ARID2
CSF3R
CTCF
CUX1
MECOM
RAD21
APC
CDKN1B
EGFR
MAP3K6
NSD1
MSH6
BCORL1

E


IDH1
DNMT3A
ASXL1
STAG2
RUNX1
SRSF2
PHF6
NPM1
FLT3
U2AF1
IDH2
JAK2
SETBP1
SMC1A
NRAS
MLL
FLCN
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BCOR
ZRSR2
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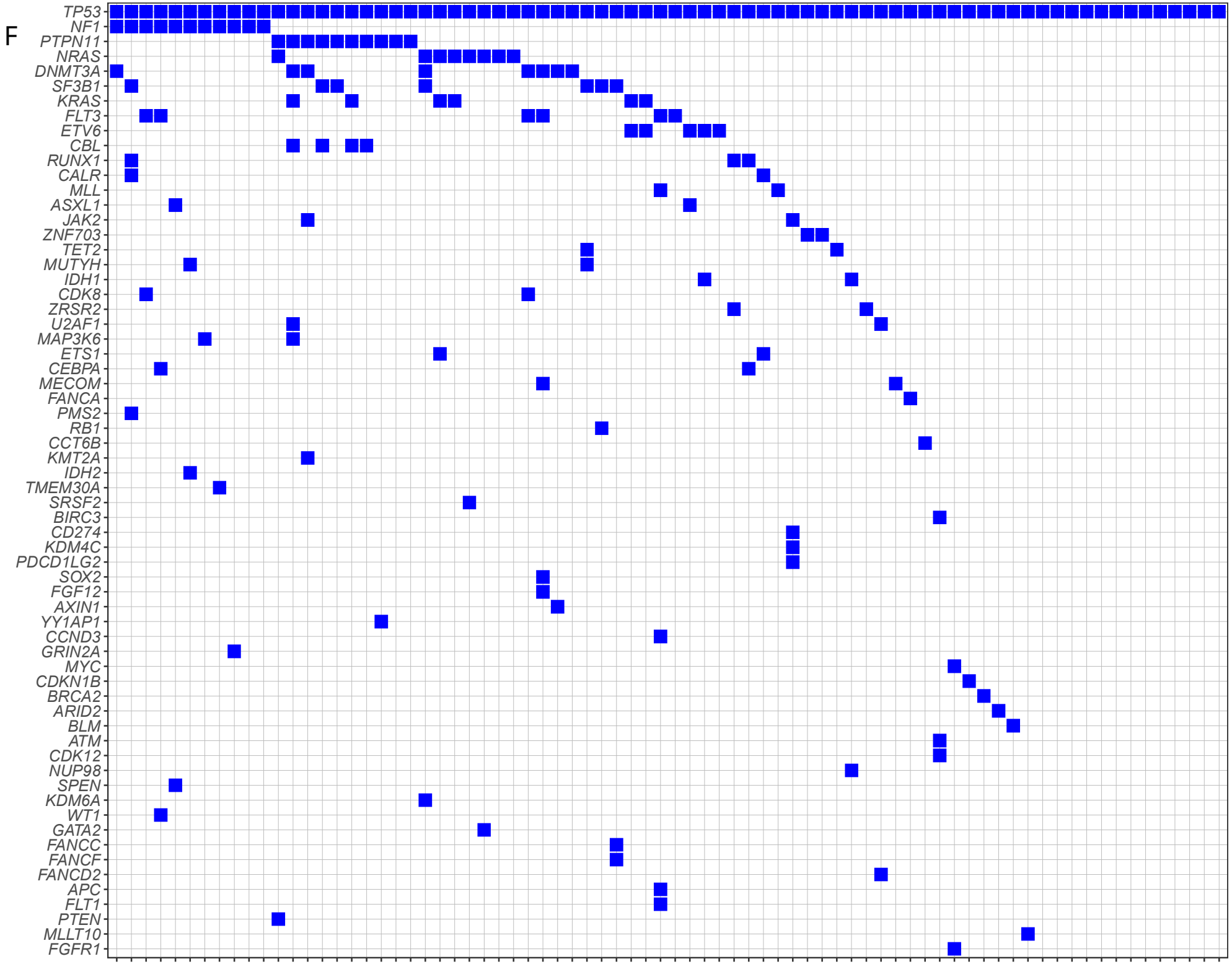
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CDK8
ZRSR2
U2AF1
MAP3K6
ETS1
CEBPA
MECOM
FANCA
PMS2
RB1
CCT6B
KMT2A
IDH2
TMEM30A
SRSF2
BIRC3
CD274
KDM4C
PDCD1LG2
SOX2
FGF12
AXIN1
YY1AP1
CCND3
GRIN2A
MYC
CDKN1B
BRCA2
ARID2
BLM
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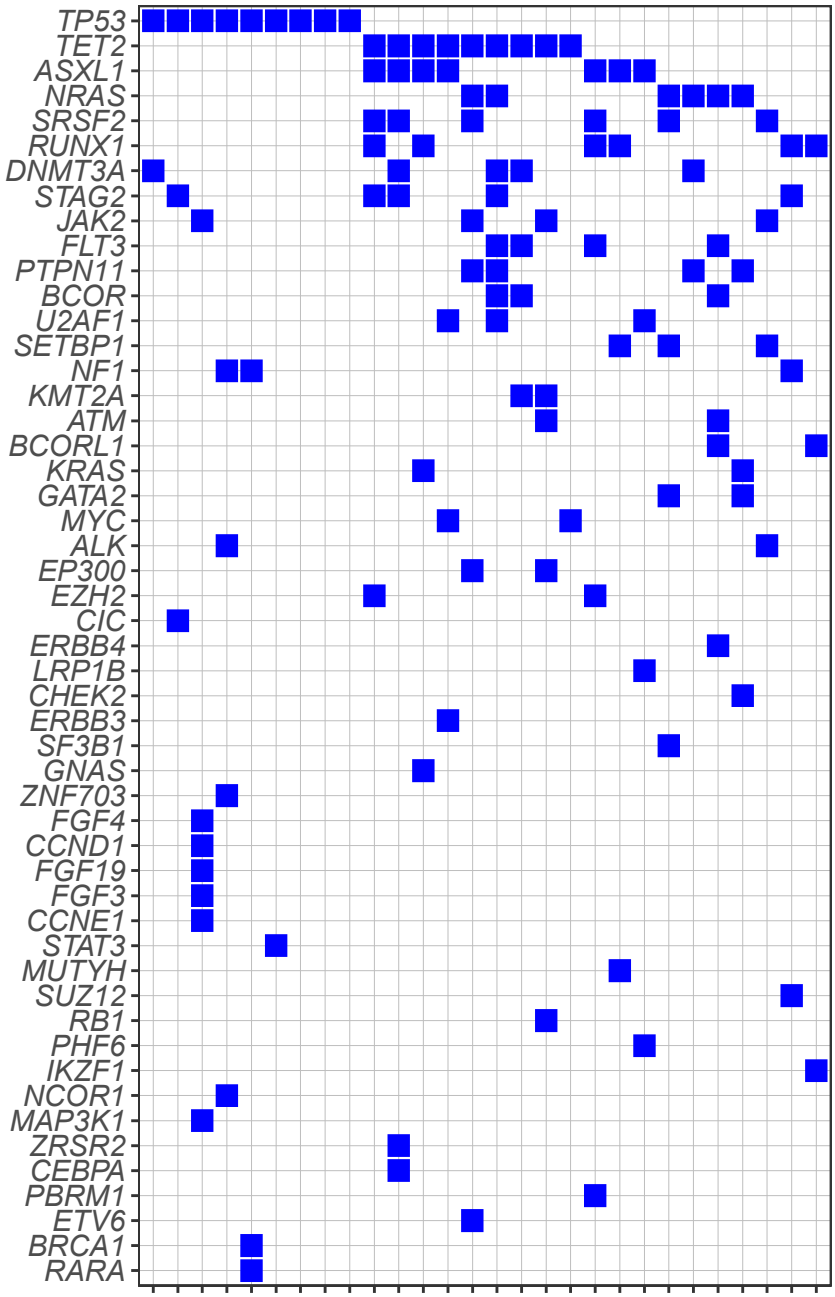
MLLT10
FGFR1

G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NF1
KMT2A
ATM
BCORL1
KRAS
GATA2
MYC
ALK
EP300
EZH2
CIC
ERBB4
LRP1B
CHEK2
ERBB3
SF3B1
GNAS
ZNF703
FGF4
CCND1
FGF19
FGF3
CCNE1
STAT3
MUTYH
SUZ12
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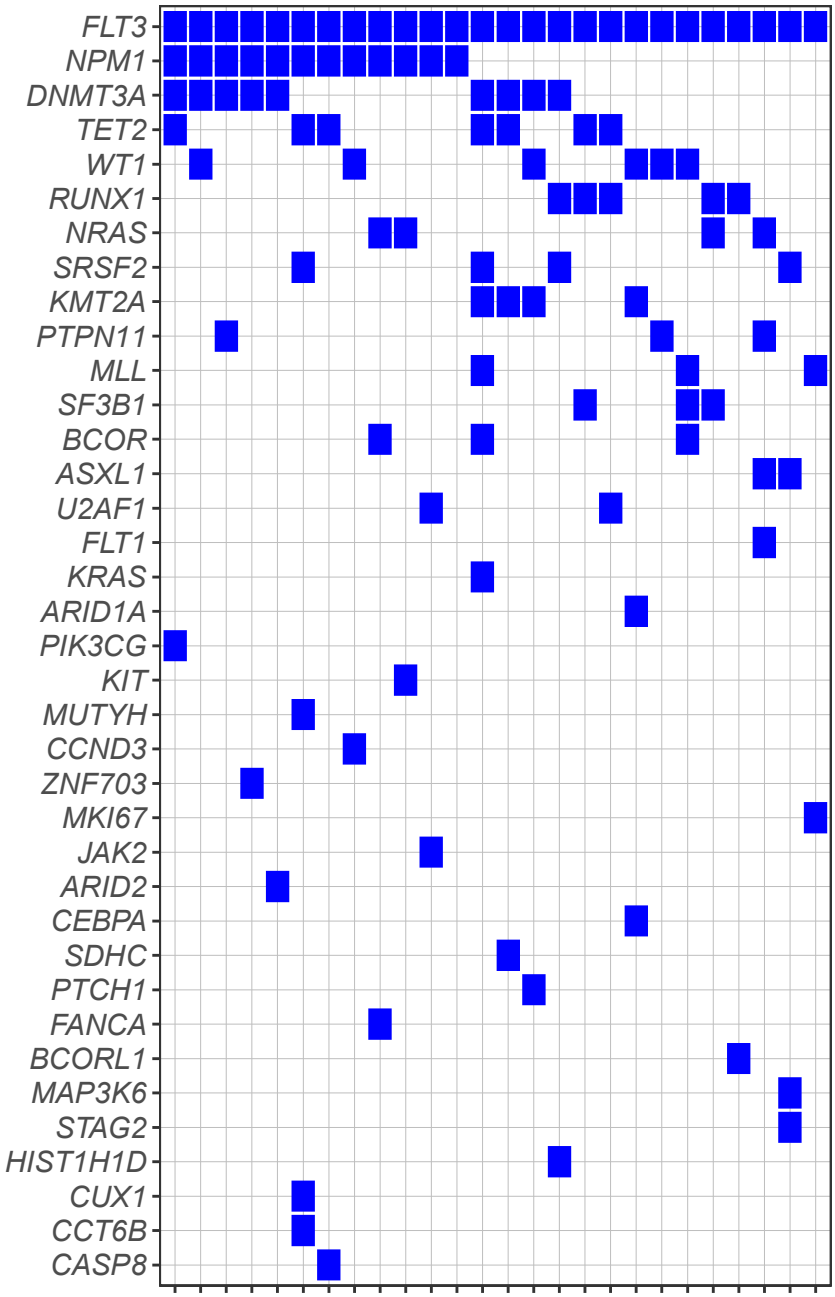
RARA

H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RUNX1
NRAS
SRSF2
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PTPN11
MLL
SF3B1
BCOR
ASXL1
U2AF1
FLT1
KRAS
ARID1A
PIK3CG
KIT
MUTYH
CCND3
ZNF703
MKI67
JAK2
ARID2
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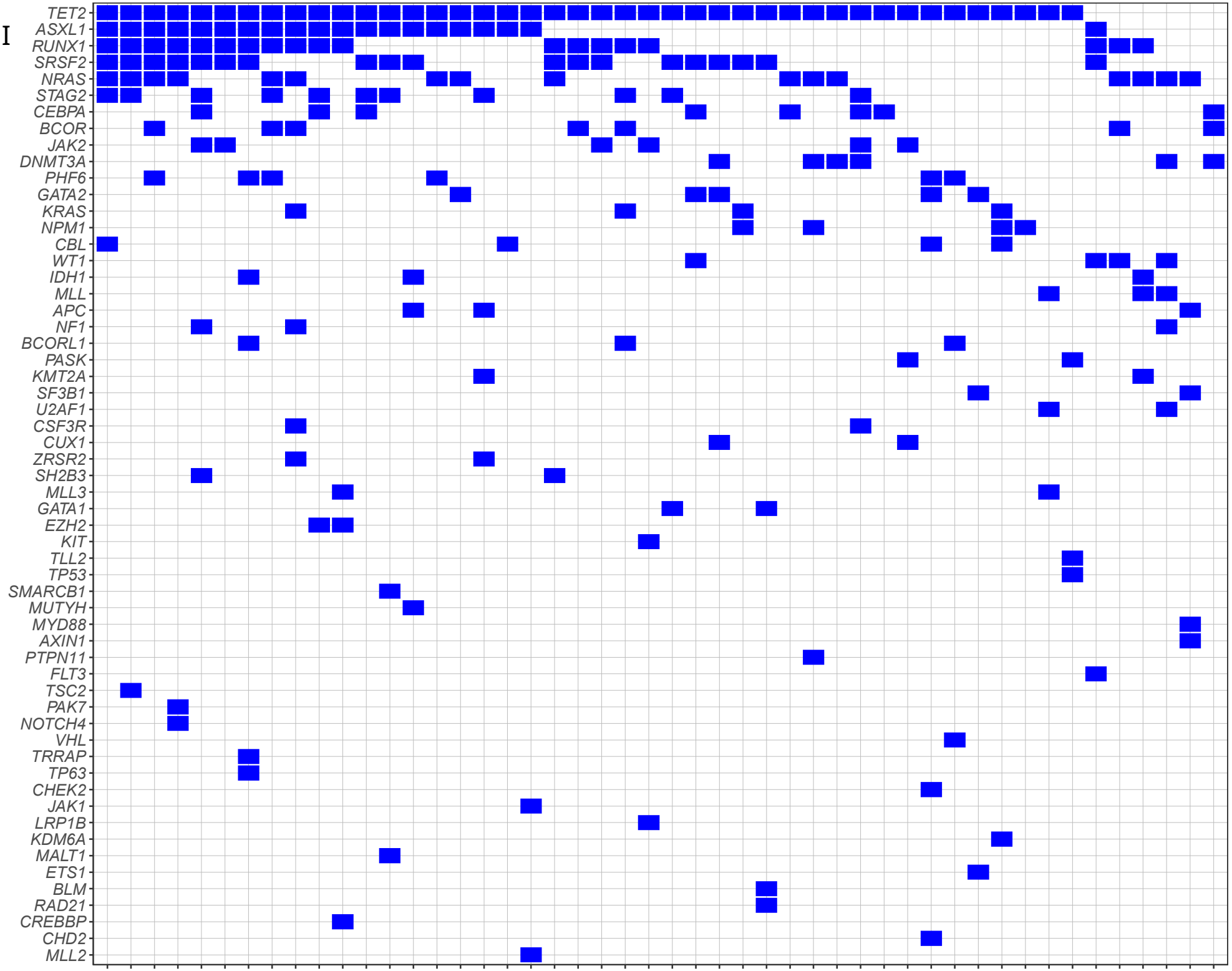
CASP8

I


TET2
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RUNX1
SRSF2
NRAS
STAG2
CEBPA
BCOR
JAK2
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PHF6
GATA2
KRAS
NPM1
CBL
WT1
IDH1
MLL
APC
NF1
BCORL1
PASK
KMT2A
SF3B1
U2AF1
CSF3R
CUX1
ZRSR2
SH2B3
MLL3
GATA1
EZH2
KIT
TLL2
TP53
SMARCB1
MUTYH
MYD88
AXIN1
PTPN11
FLT3
TSC2
PAK7
NOTCH4
VHL
TRRAP
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ETS1
BLM
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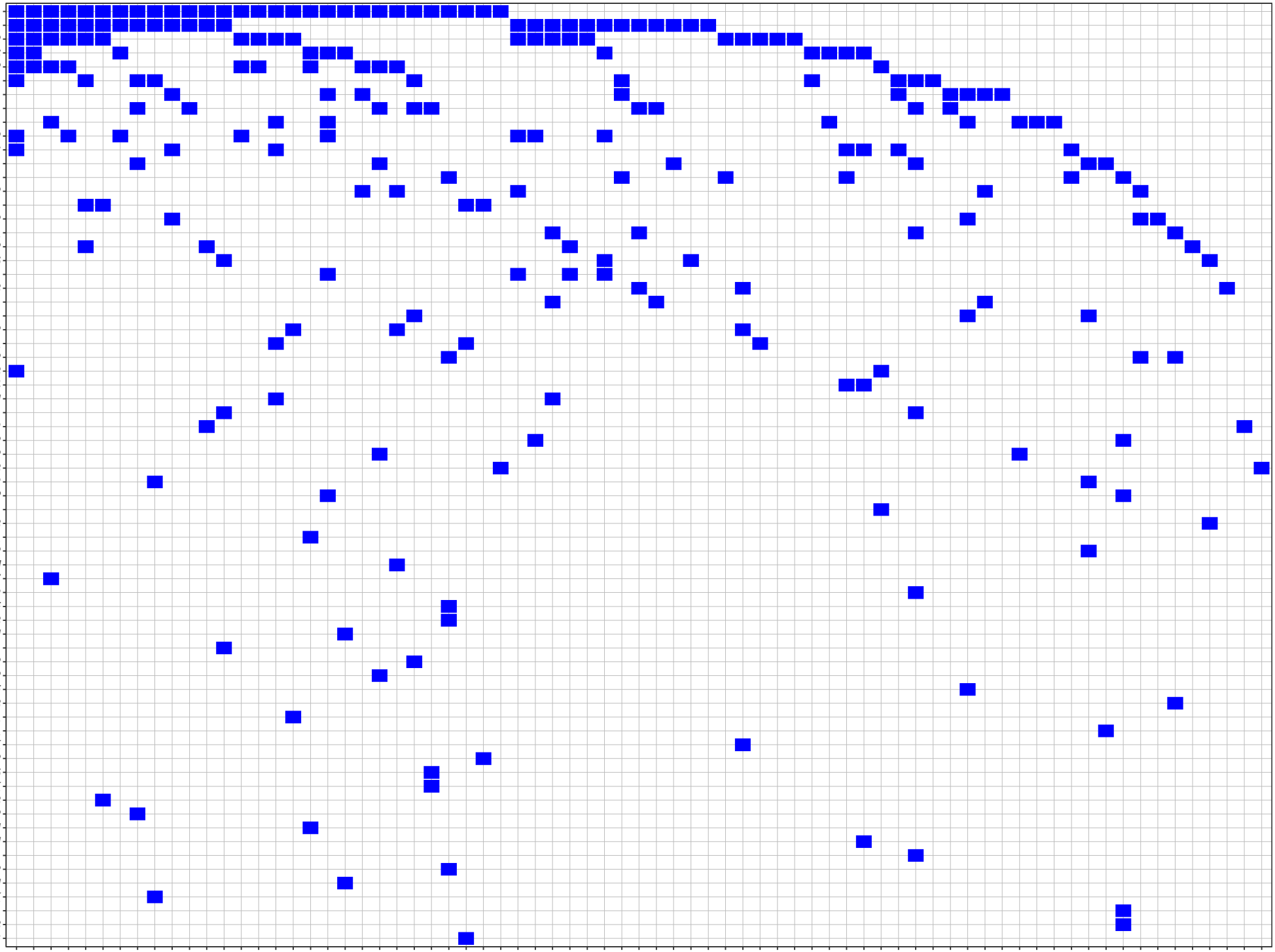
J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FLT3
NUP214
IGH
CUX1
CSF3R
MLL2
GATA2
FAT3
ZRSR2
CREBBP
NPM1
ZNF703
FANCA
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ATM
FBXW7
SUZ12
BRAF
CCND3
MUTYH
SMARCB1
CCND2
SETD2
CTCF
STAT3
RAD54L
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IGK
ARID2
MSH6
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MYST3
FANCG