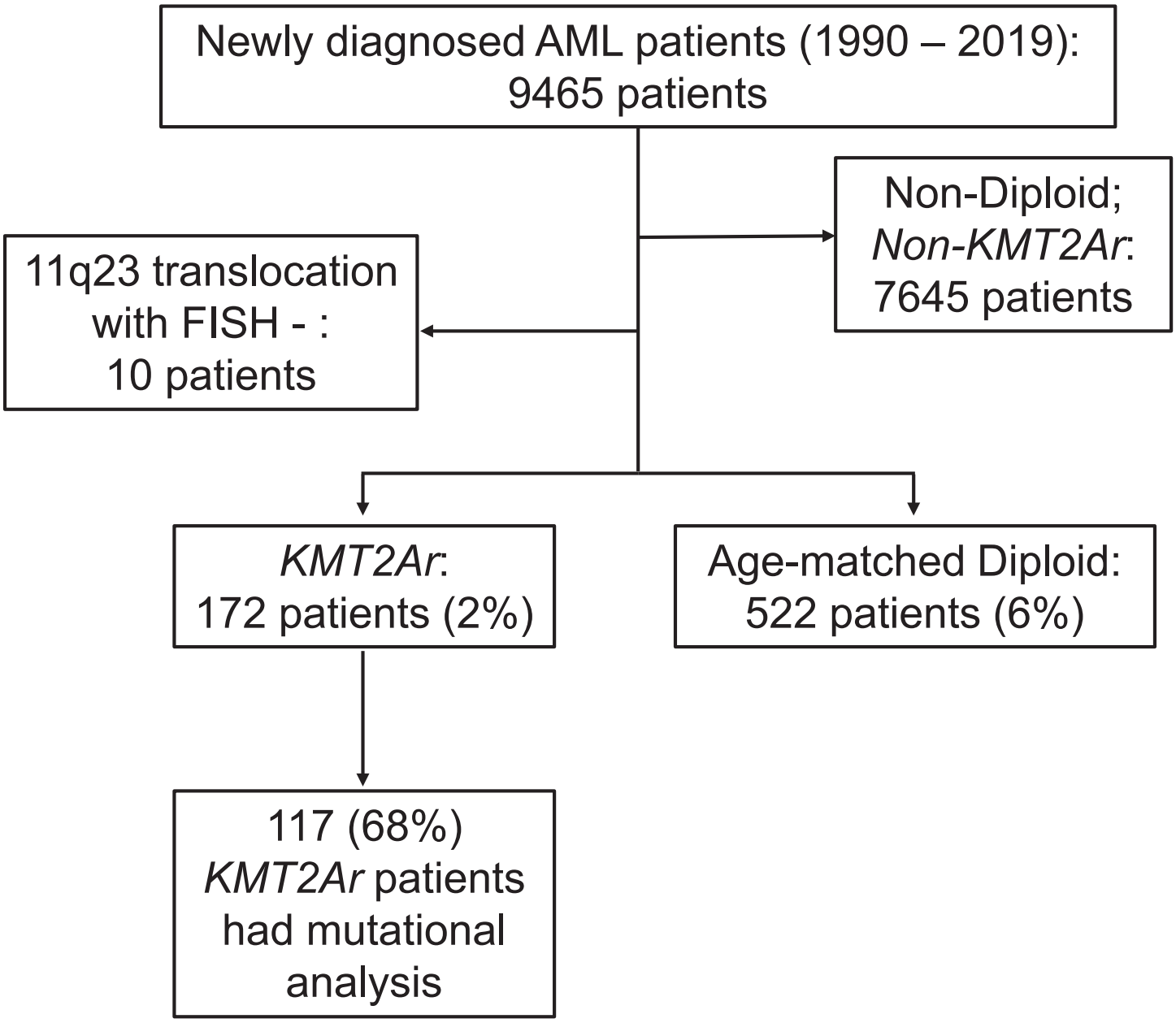
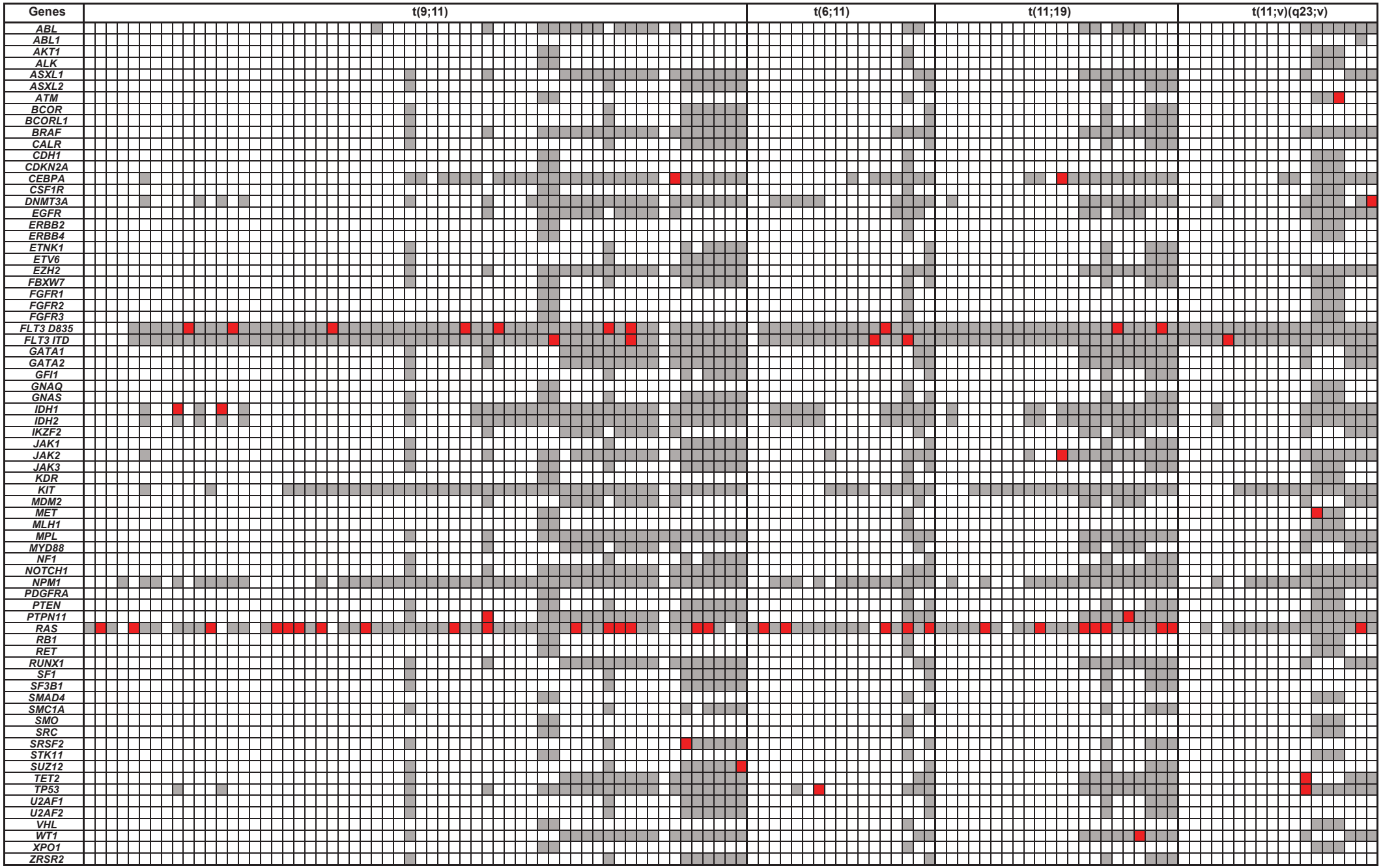
Supplemental Figure 1: Patient selection.

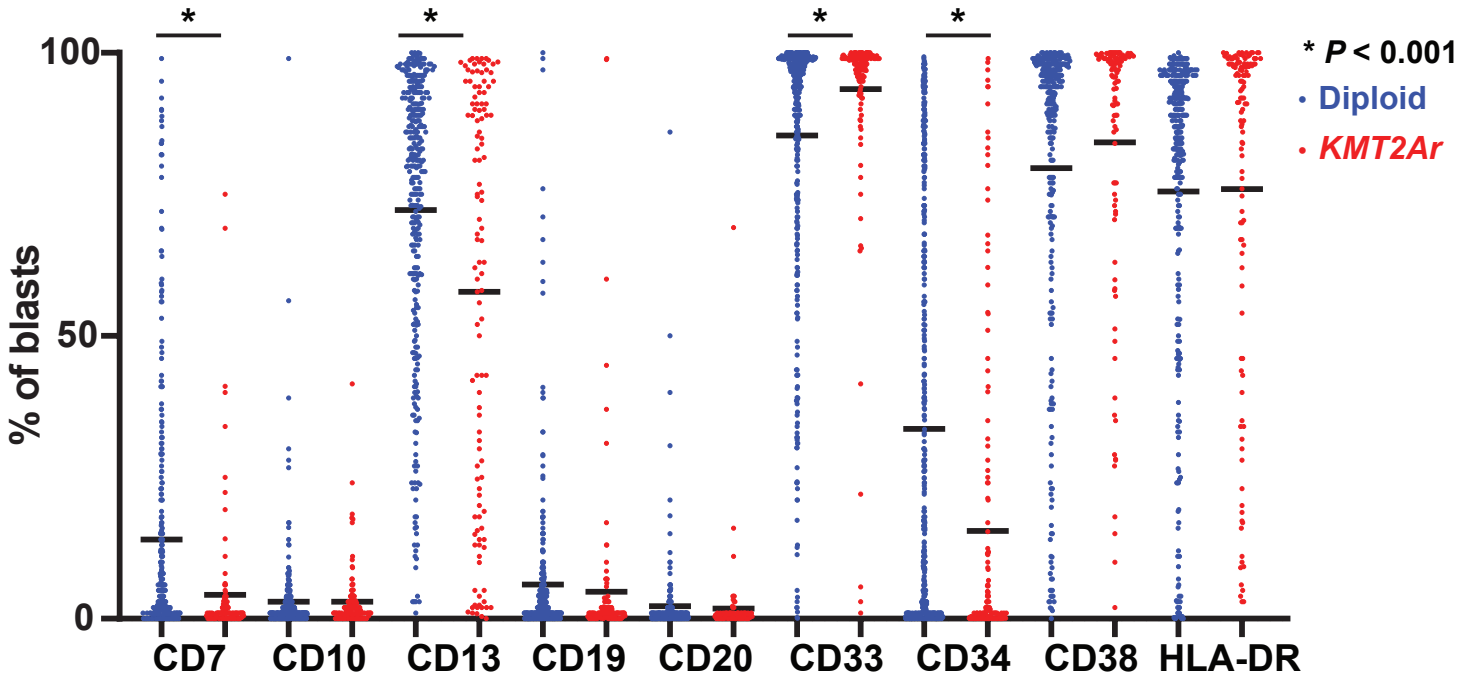


Supplemental Figure 2: Distribution of mutations per patient and by type of 11q23 translocation.

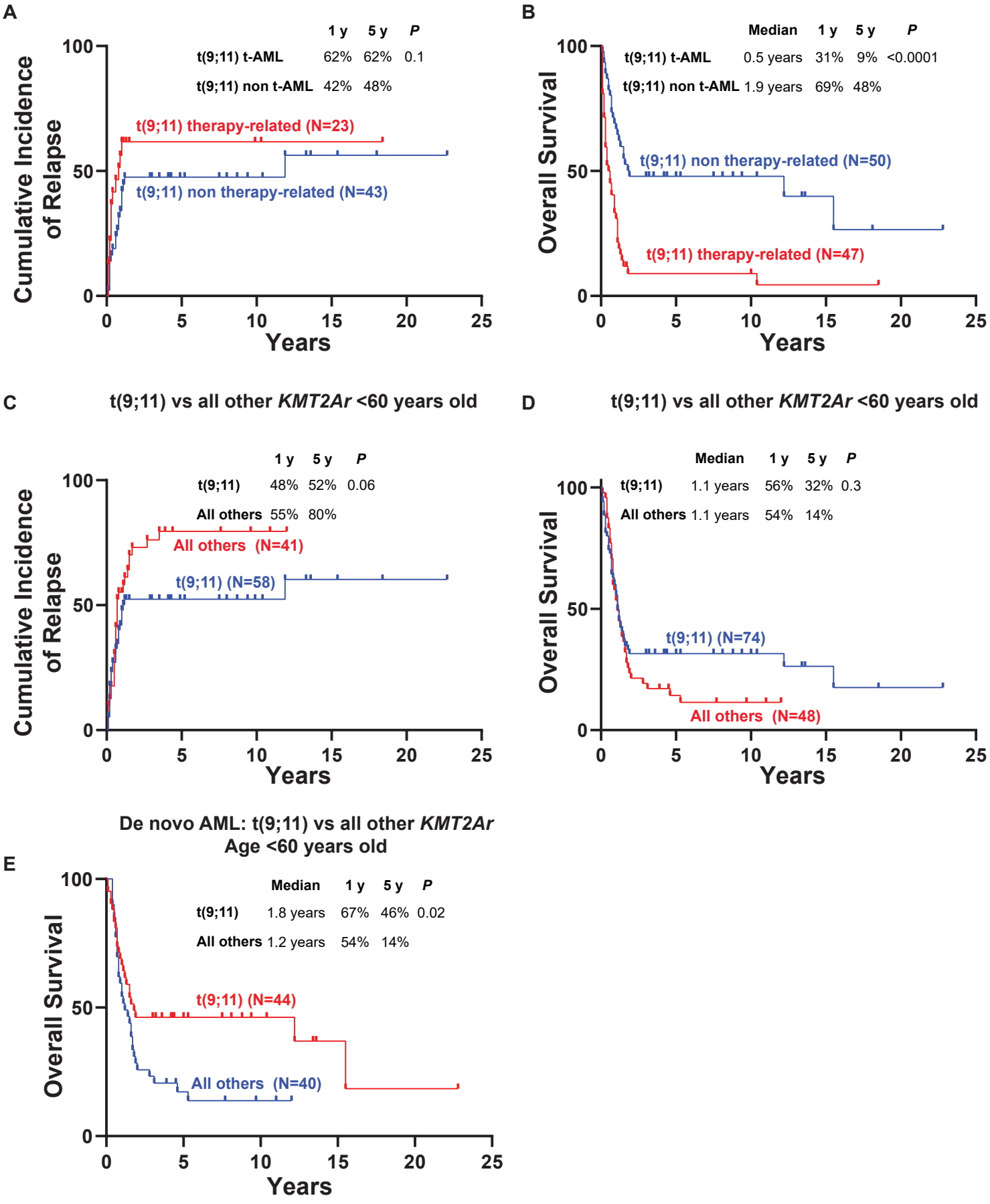


Supplemental figure 2:
Oncoprint of mutations detected in 117 patients with *KMT2Ar* AML.
Each column represents a patient and each row represents a single gene. Red, mutated; Grey, wildtype; Blank, mutational analysis not done.

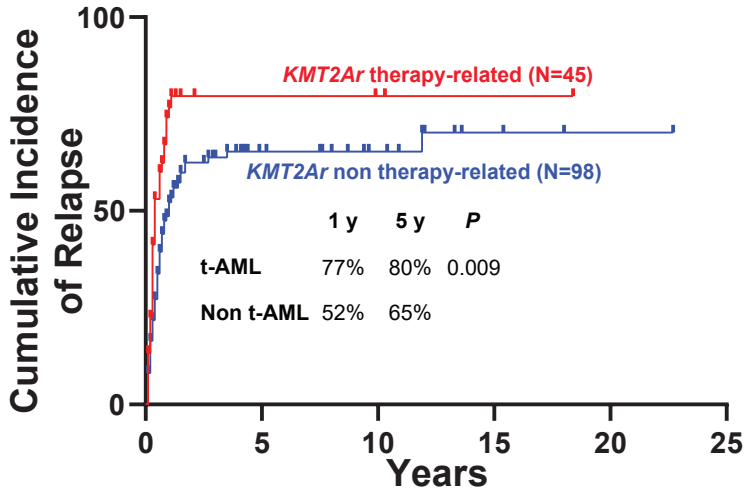
Supplemental Figure 3: Immunophenotype of *KMT2Ar* compared to diploid karyotype AML.



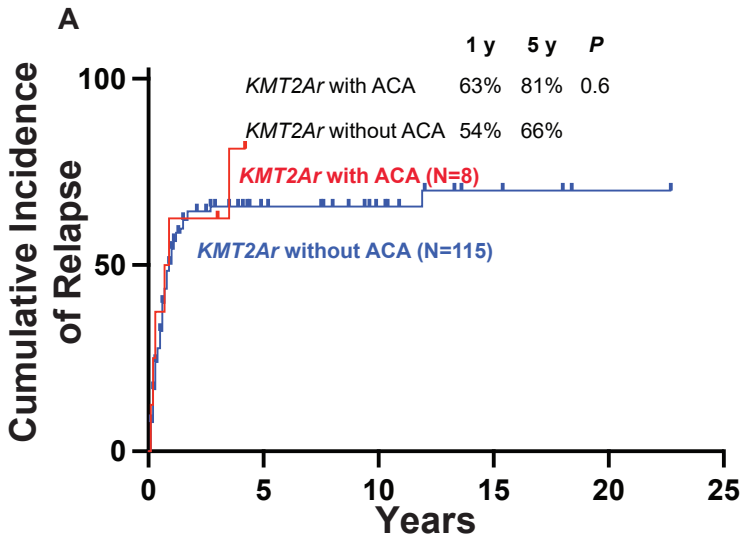
Supplemental Figure 4: Risk of relapse and overall survival of patients with t(9;11) AML.

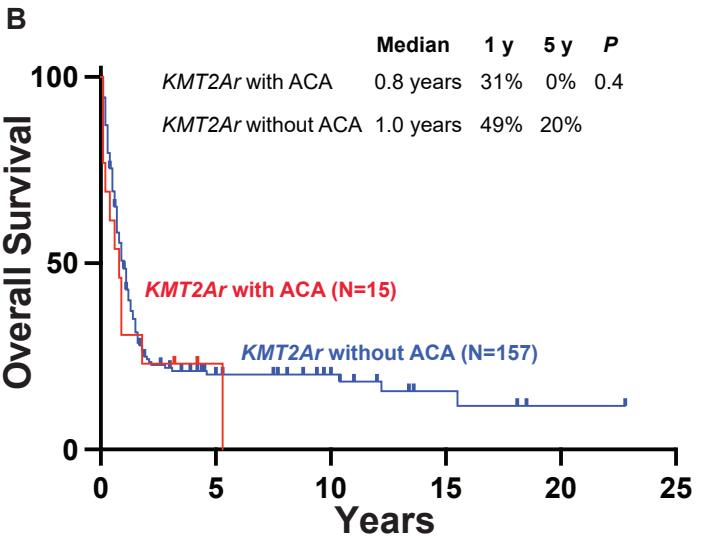


Supplemental Figure 5: Risk of relapse of patients with therapy related *KMT2Ar* AML.

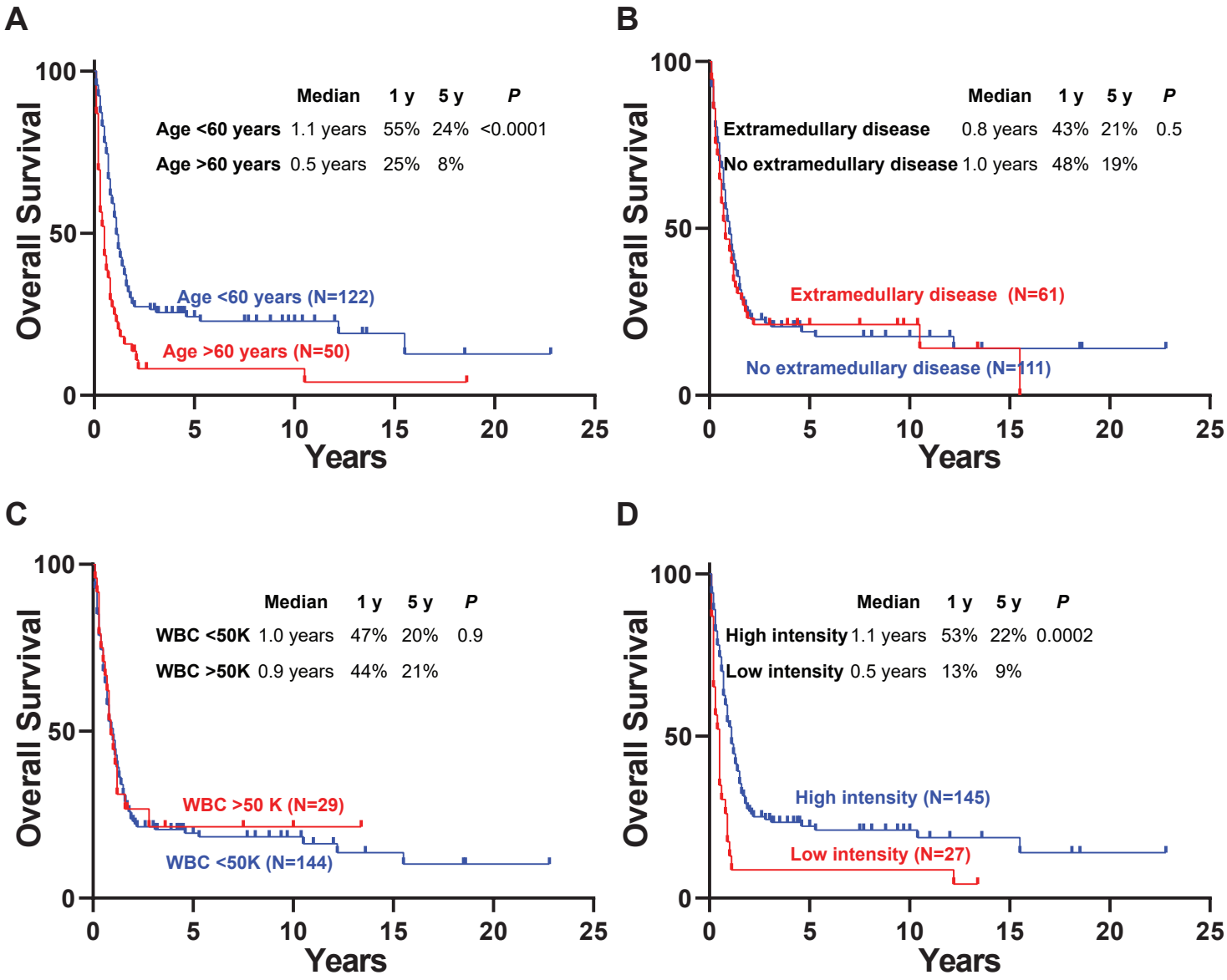


Supplemental Figure 6: Risk of relapse and overall survival of *KMT2Ar* patients with and without additional chromosomal abnormalities (ACA).

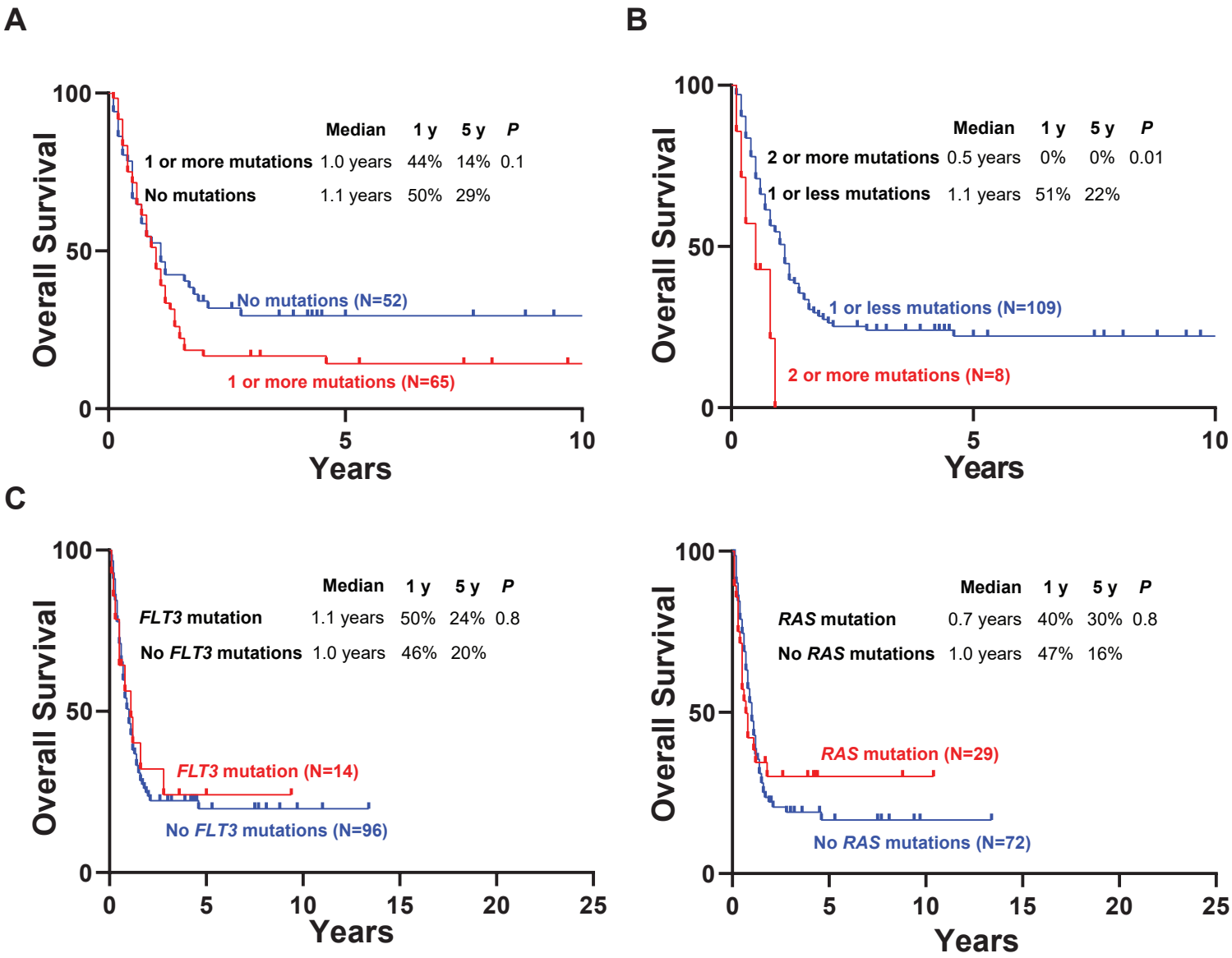




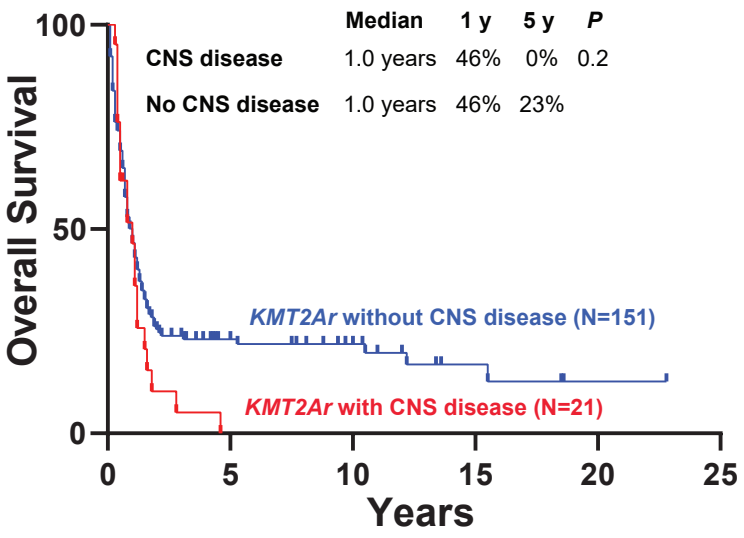
Supplemental Figure 7: Prognostic factors affecting overall survival in *KMT2Ar* AML patients.



Supplemental Figure 8: Overall survival in *KMT2Ar* AML by mutational status.

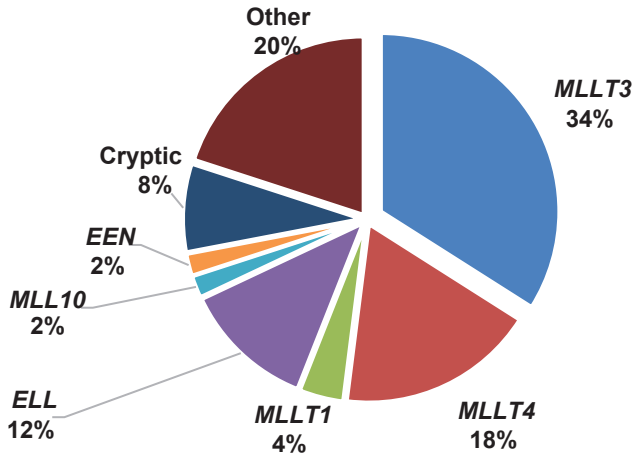


Supplemental Figure 9: Overall survival of adult patients with CNS disease in *KMT2Ar* AML.



Supplemental Figure 10: Fusion gene partners in relapsed/refractory *KMT2Ar* AML cohort.

A



B

Fusion	Cytogenetics	N (50)
KMT2A-MLLT3	t(9;11) (p21;q23)	17 (34)
KMT2A-MLLT4	t(6;11)(q27;q23)	9 (18)
KMT2A-ELL	t(11;19)(q23;p13.1)	6 (12)
KMT2A-MLLT1	t(11;19)(q23;p13.3)	2 (4)
KMT2A-EEN	t(11;19)(q23;p13)	1 (2)
KMT2A-MLLT10	t(10;11)(p12;q23)	1 (2)
Cryptic		4 (8)
Other		10 (20)

Values are N (%).

Supplemental Table 1: Panels of 28, 53, or 81 genes.

Gene	Exons (codons) tested on 81-gene panel	Exons (codons) tested on 53-gene panel	Exons (codons) tested on 28-gene panel
ANKRD26	(NM_014915) 1 (1-6)	(NM_007313): 4-6 (243-362), 7 (395-424)	(NM_005157): 1-11 (1-1004), 11 (1079-1150)
ABL1		(NM_007313): 4-6 (243-362), 7 (395-424)	(NM_005157): 1-11 (1-1004), 11 (1079-1150)
AKT1		(NM_005163): 3 (16-49)	
ALK		(NM_004304): 23 (1172-1175), 25 (1248-1275)	
APC		(NM_000038): 16 (875-918), 16 (1113-1153), 16 (1257-1297), 16 (1288-1328), 16 (1318-1357), 16 (1349-1386), 16 (1377-1575	
ASXL1	(NM_015338): 11-12 (362-1289), 12 (1299-1443), 12 (1450-1542)		(NM_015338): 2-12 (20-1542)
ASXL2	(NM_018263): 11-12 (381-1436)		
ATM		(NM_000051): 8 (353-355), 9 (409-412), 12 (601-633), 17 (846-880), 26 (1308-1331), 34 (1678-1719), 35 (1741-1773), 36 (1792-1832), 39 (1940-1973), 50 (2441-2479), 54 (2665-2670), 55 (2694-2717), 56 (2725-2756), 59 (2889-2891), 61 (2946-2950), 63 (3007-3051)	
BRAF	(NM_004333) 11 (439-478), 15 (581-620)	(NM_004333): 11 (439-471), 15 (581-606)	(NM_004333): 1 (1-23), 1-18 (34-717), 18 (725-767)
BCOR	(NM_017745): 2-3 (1-55), 4 (642-999), 4 (514-635), 4 (460-510), 4 (56-321), 4 (331-454), 5-6 (1000-1080), 7 (1137-1138), 8 (1168-1206), 8(1212-1249), 9 (1275-1340), 9-10 (1354-1366), 10-12 (1401-1547), 13-15 (1556-1640), 15 (1663-1722)		
BCORL1	(NM_021946) 1-3 (1-113), 3 (123-609), 3 (613-808), 3 (832-850), 3-4 (862-1203), 5-6 (1205-1261), 6 (1292-1323), 6-7 (1326-1378), 7(1382-1428), 7-8 (1431-1484), 9-11 (1491-1600), 11-12 (1606-1684), 12 (1687-1699), 12 (1707-1712)		
BRINP3	(NM_199051) 2-8 (1-767)		
CDH1		(NM_004360): 3 (77-117), 8 (369-379), 9 (399-439)	
CALR	(NM_004343) 9 (352-359), 9 (364-410), 9 (417)		
CSF1R		(NM_005211): 7 (297-301), 22 (926-970)	
CSF3R	(NM_156039) 14 (575-622), 17 (681-800), 17 (822-864)		
CBL	(NM_005188) 7-9 (336-477)		
CBLB	(NM_170662) 7-9 (282-397), 10 (402-469)		
CBLC	(NM_012116) 7-9 (336-454), 10 (466-475)		

CEBPA	(NM_004364) 1 (1-70), 1 (249-358), 1 (146-175), 1 (178-201)		
CTNNB1		(NM_001904): 3 (12-50)	
CREBBP	(NM_004380) 1 (1-26), 2-7 (29-559), 8 (561-608), 9-11 (615-720), 12-14 (722-837), 14-30 (840-1724), 31 (2238-2443), 31 (2051-2235), 31(2049), 31 (2011-2037), 31 (1725-1931), 31 (1967-1995)		
CUX1	(NM_181552) 2-6 (11-172), 6-9 (174-241), 10-13 (248-375), 14 (379-408)		
CRLF2	(NM_022148.2) exon 6 (codons 217-256)		
DNMT3A	(NM_022552) 8-22 (286-862), 23 (866-913)	(NM_022552): 23 (866-913)	(NM_022552): 2-23 (1-913)
DDX41	(NM_016222) 1-11 (1-410), 12-14 (420-517), 15 (522-541), 16-17 (546-623)		
EED	(NM_003797) 1-2 (1-69), 2-8 (71-287), 9-12 (289-442)		
ELANE	(NM_001972) 1-2 (5-46), 2 (69-75), 4-5 (123-268)		
ETNK1	(NM_018638) 3 (228-275)		
ETV6	(NM_001987) 1-6 (1-378), 7-8 (385-453)		
EGFR		(NM_005228): 3 (108-142), 7 (288-297), 15 (598-627), 18-20 (708-817), 21 (857-875)	(NM_005228): 1 (1-24), 2-20 (30-786), 20-23 (792-927), 23-26 (935-1043), 26-27 (1047-1061), 27-28 (1067-1211)
ERBB2		(NM_004448): 19 (754-769), 20 (772-818), 21 (839-883)	
ERBB4		(NM_005235): 3 (98-140), 4 (153-186), 6 (208-244), 7 (248-287), 8 (295-306), 9 (333-350), 15 (579-619), 23 (907-936)	
EZH2	(NM_004456) 2-5 (1-158), 5-6 (160-205), 7 (209-217), 8-19 (243-732), 20 (752)	(NM_004456): 16 (618-649)	(NM_004456): 2-5 (3-162), 6-7 (171-217), 8-20 (243-752)
FBXW7	(NM_033632) 9-12 (413-708)	(NM_033632):5 (243-278), 8 (375-394), 9 (429-471), 10 (473-508), 11 (549-583)	
FGFR1		(NM_015850): 4 (120-126)	
FGFR2		(NM_000141): 7 (250-311), 7 (302-313), 9 (362-382), 12 (521-550)	
FGFR3		(NM_000142): 7 (247-288), 9 (379-422), 14-15 (639-659), 18 (792-807)	
FLT3	(NM_004119) 11-20 (437-847)	(NM_004119): 11 (437-456), 14 (569-605), 16 (648-683), 20 (807-843)	(NM_004119): 2-24 (15-994)
GATA1	(NM_002049) 2-3 (1-84)		(NM_002049): 2-5 (1-287), 6 (291-405), 6 (407-414)
GATA2	(NM_032638) 2-5 (22-377), 5-6 (379-481)		(NM_032638): 2-6 (1-481)
GFI1	(NM_005263) 2 (2-39)		
GNA11		(NM_002067): 4-5 (172-216), 6 (255-297)	
GNAQ		(NM_002072): 4-5 (159-245), 5-6 (241-297), 6-7 (291-360), 7 (355-360)	
GNAS	(NM_000516) 8 (200-202), 11 (315-324)	(NM_000516): 8 (200-220)	
HNRNPK	(NM_002140) 3-17 (1-465)		

HNF1A		(NM_000545): 3 (205-238), 4 (271-314)	
HRAS	(NM_005343) 2-3 (1-59), 3-4 (87-135), 4 (137-150)	(NM_005343): 2 (1-15), 3 (38-63)	(NM_005343): 2-5 (1-190)
IDH1	(NM_005896) 4 (132-133)	(NM_005896): 3-10 (1-415)	(NM_005896): 3-10 (1-415)
IDH2	NM_002168) 4 (125-178)	(NM_002168): 4 (125-178)	(NM_002168): 1 (1-14), 1-11 (26-453)
IKZF2	(NM_006060) 2-8 (1-377), 8 (383-392), 8 (403-430), 8 (445), 8 (481-493)		(NM_016260): 2-8 (1-527)
IL2RG	(NM_000206) 1-2 (1-45), 2-4 (51-195), 5-8 (199-339)		
IL7R	(NM_002185) 5-7 (180-292)		
JAK1	(NM_002227) 3-9 (3-445), 10 (447-465), 10-22 (470-1023), 22-24 (1026-1123)		
JAK2	(NM_004972) 10 (405-442), 12-14 (505-622), 16 (665-711), 18 (762-812)	(NM_004972): 14 (615-622)	(NM_004972): 3-18 (1-806), 19-25 (812-1133)
JAK3	(NM_000215) 2-6 (1-284), 7-13 (288-590), 14-23 (596-1069)	(NM_000215): 13 (568-573), 16 (683-723)	
KDM6A	(NM_021140) 2-9 (54-223), 9-16 (228-631), 17-19 (642-971), 20-21 (980-1070), 22-29 (1080-1402)		
KDR		(NM_002253); 6 (220-248), 7 (267-276), 11 (471-476), 19 (872-874), 21 (946-985), 26 (1135-1146), 27 (1171-1211), 30 (1308-1357)	
KIT	(NM_000222) 8-9 (411-514), 11 (550-592), 17 (788-828)	(NM_000222): 2 (51-93), 9-10 (502-547), 10-11 (540-592), 13 (641-664), 14 (670-712), 15 (714-745), 17 (815-828), 18 (838-866)	(NM_000222): 1-6 (1-334), 6-21 (367-977)
KLHL6		(NM_130446): 1 (1-98)	
KRAS	(NM_004985) 2-4 (1-150)	(NM_004985): 2 (1-22), 3 (38-63), 4 (103-147)	(NM_004985): 2-5 (1-189)
MAP2K1	(NM_002755) 2 (27-90), 3 (98-146)		
MDM2			(NM_002392): 1-11 (1-498)
MET		(NM_001127500): 2 (168-209), 2 (375-400), 14 (1008-1028), 16 (1110-1132), 19 (1247-1284)	
MLH1		(NM_000249): 12 (383-426)	
MLL(KMT2A)	(NM_005933) 2 (145-168), 3-4 (176-1075), 4 (1081-1112), 5 (1117-1184), 6 (1190-1212), 7 (1224-1325), 8-13 (1338-1560), 14-15 (1566-1665), 27 (2186-2195), 27 (2201-2355), 27 (2373-2452), 27 (2472-3215), 27 (3223-3324), 27 (3339-3575)		(NM_005933): 1-5 (103-1190), 6-36 (1207-3970)
MPL	(NM_005373):10 (490-522), 12 (552-636)	(NM_005373): 10 (514-522)	(NM_005373): 1-9 (1-488), 10-12 (490-636)
MYD88		(NM_002468): 1 (1-6), 1-5 (15-310)	
NF1	(NM_001042492) 2-5 (21-189), 6 (201-218), 8-13 (244-467), 13-17 (478-667), 18 (674-728), 18-22 (746-992), 23-24 (997-1066), 25-26 (1082-1146), 26-31 (1160-1378), 31-35 (1382-1549),		

	35-38 (1564-1868), 39 (1870-1884), 39-47 (1886-2322), 47-52 (2325-2555), 52-58 (2568-2840)		
NOTCH1	(NM_017617) 26 (1529-1594), 26-28 (1602-1795), 34 (2550-2556), 34 (2290-2543), 34 (2069-2229), 34 (2234-2273), 34 (2550-2556), 34(2290-2543), 34 (2069-2229), 34 (2234-2273)	(NM_017617): 26 (1562-1601), 27 (1673-1679)	(NM_017617): 2-31 (21-1893), 31-34 (1902-2286), 34 (2289-2552)
NPM1	(NM_002520) 11 (283-295)	(NM_002520): 11 (283-295)	(NM_002520): 1-7 (1-181), 7-11 (187-295)
NRAS	(NM_002524) 2-4 (1-150)	(NM_002524): 2 (1-18), 3 (38-62)	(NM_002524): 2-5 (1-190)
PAX5	(NM_016734) 1-10 (14-392)		
PDGFRA		(NM_006206): 12 (552-592), 14 (659-668), 15 (673-717), 18 (823-854)	
PHF6	(NM_032458) 2-3 (1-78), 4-10 (81-366)		
PIGA	(NM_002641) 2 (1-6), 2-5 (16-396), 6 (399-418), 6 (422-485)		
PML	(NM_033238) 3 (201-255)		
PRPF40B	(NM_001031698) 2-19 (2-609), 19 (611-626), 20 (629-658), 20-26 (661-893)		
PIK3CA		(NM_006218): 2 (83-118), 5 (345-353), 8 (418-445), 10 (538-555), 14 (701-729), 21 (988-1069)	
PTPN11	(NM_002834) 3-4 (46-125), 7 (253-285), 12 (460-462), 12-13 (465-533)	(NM_002834): 3 (59-104), 13 (501-533)	(NM_002834): 1-4 (1-157), 5-15 (176-594)
PTEN	(NM_000314) 7-8 (212-285), 8 (290-342)	(NM_000314): 1 (5-27), 3 (67-70), 6 (170-210), 7 (212-266), 8 (287-342)	
RAD21	(NM_006265) 2-13 (1-560), 14 (569-632)		
RARA	(NM_000964) 6-7 (211-338)		
RB1		(NM_000321): 4 (127-158), 6 (199-203), 11 (357-376), 18 (570-605), 20 (659-700), 21 (703-733), 22 (746-775)	
RET		(NM_020975): 10-11 (610-667), 13 (766-798), 15 (880-910), 16 (918-934)	
RUNX1	(NM_001754) 2-4 (1-70), 4-9 (79-437)		(NM_001754): 2-4 (1-70), 4-9 (73-437)
SETBP1	(NM_015559) 4 (838-885)		
SF1	(NM_004630) 2-12 (11-524), 13 (528-578), 13 (582-640)		
SF3A1	(NM_005877) 1-7 (1-322), 7-9 (329-424), 9-12 (427-634), 13-16 (651-794)		
SF3B1	(NM_012433) 13-16 (574-790)		
SH2B3	(NM_005475) 2 (1-39), 2 (43-99), 2 (132-150), 2 (158-164), 2-8 (212-576)		
SMC1A	(NM_006306) 1-5 (13-283), 6-7 (285-415), 8-14 (419-771), 15-19 (775-976), 20-22 (992-1146), 23-24		

	(1148-1206), 25 (1217-1234)		
SMC3	(NM_005445) 1 (1-5), 2-6 (19-110), 6-16 (113-504), 16-17 (507-580), 17-25 (591-975), 25-29 (979-1217)		
SRSF2	(NM_003016) 1 (1-38), 1 (45-121)		
STAG1	(NM_005862) 2 (1-5), 3-20 (10-703), 21-22 (718-738), 22-27 (740-953), 27-34 (955-1259)		
STAG2	(NM_006603) 2-15 (1-512), 16 (521-534), 16-21 (541-711), 21-33 (714-1232)		
STAT3	(NM_139276) 17 (489-503), 18-22 (534-715)		
SMAD4		(NM_005359): 3 (119-142), 5 (167-208), 6 (243-263), 8 (310-319), 9 (329-373), 10 (385-424), 11 (443-480), 12 (496-535)	
SMARCB1		(NM_003073): 2 (39-78), 4 (156-167), 5 (199-210)	
STAT5A	(NM_003152) 3-6 (1-177), 6-7 (181-206), 8-9 (266-286), 9-20 (315-795)		
STAT5B	(NM_012448) 16 (636-693)		
SMO		(NM_005631): 3 (197-242), 5 (323-366), 6 (403-422), 9 (533-551)	
SUZ12	(NM_015355) 1 (20-44), 1 (46-84), 2 (92-107), 4-5 (129-169), 7-16 (198-740)		
SRC		(NM_005417): 14 (530-537)	
STK11		(NM_000455): (36-77), 4-5 (193-211), 6 (261-288), 8 (332-370)	
TET2	(NM_001127208) 3 (1-77), 3 (91-826), 3 (829-853), 3-11 (867-2003) (NM_000546) 2 (1-25), 4 (80-125), 5-11 (134-394)		(NM_001127208): 3 (1-854), 3-11 (866-2003)
TP53	(NM_000546) 2 (1-25), 4 (80-125), 5 (134-187), 6-11 (190-394)	(NM_000546): 2 (1-12), 4 (69-112), 5 (126-186), 5-6 (181-192), 6 (187-223), 6-7 (214-253), 8 (267-306), 10 (332-342)	(NM_000546): 2-11 (1-394)
TERC	81 gene panel		
TERT	(NM_198253) 1 (1-24), 2 (349-525), 2 (80-164), 2 (258-342), 3-4 (525-630), 4-5 (633-663), 5 (675-677), 6 (711-749), 6-8 (753-800), 8-11 (805-925), 11-16 (933-1133)		
U2AF1	(NM_006758) 2 (15-44), 6 (117-161)		
U2AF2	(NM_007279) 1 (1-17), 3-5 (62-161), 6-12 (163-437), 12 (441-473)		
VHL		(NM_000551): (88-114), 2 (129-155), 3 (157-200)	
WT1	(NM_024426) 1 (187-216), 1 (179-184), 1 (2-44), 1 (122-165), 2-10 (216-518)		(NM_024426): 1 (1-59, 72-105, 122-216), 2-10 (216-518)
XPO1		(NM_003400) 14-15 (501-575)	

ZRSR2	(NM_005089) 1-3 (1-68), 4 (71-90), 6-8 (134-201), 8 (212-257), 10-11 (276-417), 11 (476-483)

Supplemental Table 2: Baseline characteristics of relapsed/refractory adult AML with *KMT2Ar*.

Characteristic	*KMT2Ar*	Age-matched diploid	*P*
Patients, no.	50	177	
Median age, years (range)	47 (22-75)	54 (10-85)	0.07
Female, no. (%)	28 (56)	79 (45)	0.2
Monocytic phenotype, no. (%)	15 (30)	44 (25)	0.5
WBC, median x 10^9/L (range)	4.3 (0-135)	8 (0-250)	0.03
Platelets, median x 10^9/L (range)	54 (7-358)	56 (1-497)	0.8
BM blast %, median (range)	51 (0-94)	48 (15-96)	0.4
High intensity treatment, no. (%)	46 (92)	138 (78)	0.03
Low intensity treatment, no. (%)	4 (8)	39 (22)	
Allo-HSCT, no. (%)	18 (36)	34 (19)	0.02

High intensity treatment includes treatment with the combination of cytarabine and idarubicin or the addition of a nucleoside analog to the combination. Low intensity treatment includes treatment with hypomethylating agents, low-dose cytarabine, or targeted therapies.
WBC, white blood cell; BM, bone marrow; LDH, lactate dehydrogenase; Allo-HSCT, allogeneic hematopoietic stem cell transplant; t-aml; therapy related AML.
P: Kruskal-Wallis or Fisher exact test.

Supplemental Table 3: Karyotype of 10 patients with less common *KMT2A* rearrangements who constitute the "Other" group in relapse/refractory cohort.

Age and Sex	Karyotype
31/F	(12)46XX,3q-,t(11q;15q);(9)45-46",+other changes;(4)+6
43/F	"47,XX,t(3;7)(p21;p22),t(4;10;15)(q21;p13;q15),+6,add(6)(q21),del(9)(q13q22),t(11;22)(q23;q11.2)[13]
58/F	45,XX,t(5;11)(q35;q23),-10,ider(17)(q10)del(17)(q11.2q21)[11];46,XX[9]
75/M	47,XY,t(3;11)(q12;q23),+8[2]; 47,idem,del(2)(q33)[18]
50/F	46,XX,t(8;11)(q13;p12)[1];46,XX[19]
5 patients	Unknown karyotype

Supplemental Table 4: Treatments for newly diagnosed *KMT2Ar* AML patients.

Treatment regimen	N (%)
High intensity	145 (84)
IA (Idarubicin + Cytarabine)	60 (41)
CLIA (Cladribine + IA)	9 (6)
FIA (Fludarabine + IA)	11 (8)
CIA (Clofarabine + IA)	17 (12)
FLAG-Ida + venetoclax	2 (1)
CLIA + venetoclax	3 (2)
Other	43 (30)
Low intensity	27 (16)
LDAC	2 (7)
HMA	9 (33)
HMA + venetoclax	5 (19)
Other	11 (41)

LDAC, low-dose cytarabine; HMA, hypomethylating agents.
Midostaurin was added to therapy in 3 of 14 patients with *KMT2Ar* and *FLT3* mutations.
Other treatments include investigational agents as single agents or in combinations with high intensity chemotherapy or less commonly used regimens.

Supplemental Table 5: Karyotype of 17 patients with less common *KMT2A* rearrangements who constitute the "Other" group.

Age and Sex	Karyotype
27/M	(25)46XY,t(11q-;17q+)(q23;q25)
31/M	(17)46XY,t(10p-;11q+);(7)46XY,1p+,t(10p-;11q+);(1)46XY
51/F	(19)47XX,t(7;11)(q11.2;q23),+8;(2)DIP
21/M	t(x;11)(q22;q23)
48/F	47,XY,t(3;11)(q12;q23),+8[2]; 47,idem,del(2)(q33)[18]
51/F	t(11;22)(q23;q12)
40/F	46XX,DER(2)t(2;11)(q31;q23)[20]
73/M	t(1;11)(p32;q23)
54/F	t(11;17)(q23;q25)
64/F	t(2;11)(p21;q23),
31/F	t(7;11)(q32;q23)
50/F	t(1;11)(p34;q13),
70/M	t(11;16)(q23;p13.3),
32/M	t(11;17)(q23;q12),
50/M	t(11;17)(q23;q25)
71/M	t(11;15)(q23;q14),
55/M	t(11;17)(q23;q12),

Supplemental Table 6: Baseline characteristics of newly diagnosed *KMT2Ar* AML by subgroups.

Characteristic	t(9;11)	t(6;11)	*P*	t(11;19)	*P*	t(11;v)(q23;v)	*P*
Patients, no.	97	19		34		22	
Median age, years (range)	52 (17-82)	54 (22-85)	0.8	52 (23-83)	0.7	52 (20-73)	0.9
Female, no. (%)	65 (67)	11 (58)	0.4	18 (53)	0.2	10 (45)	0.09
Monocytic phenotype, no. (%)	73 (75)	14 (74)	0.9	19 (56)	**0.048**	10 (45)	**0.009**
WBC, median x 10^9/L (range)	9 (1-270)	9 (1-134)	0.9	9 (1-111)	0.9	9 (1-106)	0.9
Platelets, median x 10^9/L (range)	48 (4-235)	49 (9-155)	0.9	49 (10-187)	0.9	49 (3-279)	0.9
BM blast %, median (range)	76 (20-98)	76 (22-94)	0.9	75 (22-92)	0.9	76 (21-94)	0.9
t-AML, no. (%)	47 (48)	5 (26)	0.08	10 (29)	0.07	7 (32)	0.2
High intensity treatment, no. (%)	82 (85)	17 (89)	0.7	26 (76)	0.3	20 (91)	0.7
Low intensity treatment, no. (%)	15 (15)	2 (11)		8 (24)		2 (9)	
Allo-HSCT, no. (%)	26 (27)	8 (42)	0.3	7 (21)	0.6	5 (23)	0.8

High intensity treatment includes treatment with the combination of cytarabine and idarubicin or the addition of a nucleoside analog to the combination. Low intensity treatment includes treatment with hypomethylating agents, low-dose cytarabine, or targeted therapies.

WBC, white blood cell; BM, bone marrow; LDH, lactate dehydrogenase; Allo-HSCT, allogeneic hematopoietic stem cell transplant; t-aml; therapy related AML.

P: Kruskal-Wallis or Fisher exact test.

Supplemental Table 7: Frequency of mutations by 11q23 translocation.

	t(9;11)	t(6;11)	*P*	t(11;19)	*P*	t(11;v)(q23;v)	*P*
RAS	16/52 (31)	5/15 (33)	0.9	7/21 (33)	0.9	1/15 (7)	0.09
FLT3	8/55 (15)	3/16 (19)	0.7	2/22 (9)	0.7	1/17 (6)	0.7
PTPN11	1/20 (5)	0/3 (0)	0.9	1/9 (11)	0.5	0/7 (0)	0.9
TP53	0/22 (0)	1/5 (20)	0.2	0/9 (0)	0.9	1/7 (14)	0.2
CEBPA	1/29 (3)	0/7 (0)	0.9	1/13 (8)	0.5	0/8 (0)	0.9
IDH 1/2	2/30 (7)	0/10 (0)	0.9	0/14 (0)	0.9	0/8 (0)	0.9
WT1	0/17 (0)	0/2 (0)	0.9	1/14 (7)	0.5	0/4 (0)	0.9

Values are mutated/tested (%). Subgroups were compared to t(9;11).

Supplemental Table 8: Responses of newly diagnosed *KMT2Ar* AML by subgroups.

Best Response	t(9;11)	t(6;11)	*P*	t(11;19)	*P*	t(11;v)(q23;v)	*P*
N	97	19		34		22	
CR	63 (65)	11 (58)	0.9	23 (68)	0.7	16 (73)	0.1
CRi	3 (3)	2 (11)		2 (6)		3 (14)	
CR+CRi	66 (68)	13 (68)		25 (74)		19 (86)	
No response	31 (32)	6 (32)		9 (27)		3 (14)	
MRD negative by MFC	10/11 (91)	1/2 (50)	0.3	3/7 (43)	0.047	3/5 (60)	0.2

Values are n (%).
CR, complete remission; CRi, complete remission with incomplete hematologic recovery; MRD, minimal residual disease assessed by multiparameter flow cytometry (MFC) following induction in evaluable patients.
P: Kruskal-Wallis or Fisher exact test. All subgroups were compared to t(9;11).

Supplemental Table 9: Responses by lines of therapy for adults with AML.

	1st Line			2nd Line			≥ 3rd Line		
	KMT2Ar	**Diploid**	***P***	***KMT2Ar***	**Diploid**	***P***	***KMT2Ar***	**Diploid**	***P***
N	172	522		91	178		217	112	
CR	113 (66)	403 (77)	0.01	31 (34)	61 (34)	0.8	11 (5)	17 (15)	< 0.001
CRi	10 (6)	18 (4)		8 (9)	19 (11)		9 (4)	18 (16)	
CR+CRi	123 (72)	421 (81)		39 (43)	80 (45)		20 (9)	35 (31)	
No response	49 (28)	101 (19)		52 (57)	98 (55)		197 (91)	77 (69)	
MRD negative by MFC	17/25 (68)	90/132 (68)	0.9	12/16 (75)	16/24 (67)	0.7	1/3 (33)	8/9 (89)	0.1

Values are n (%).
CR, complete remission; CRi, complete remission with incomplete hematologic recovery; MRD, minimal residual disease assessed by multiparameter flow cytometry (MFC) following induction in evaluable patients.

Supplemental Table 10: Variables associated with CNS disease in adults with KMT2Ar AML.

Variables	CNS +	CNS-	*P*
Patients, no. (%)	20 (12)	152 (88)	
WBC, median x 10^9/L (range)	8.5 (1-108)	9.1 (1-270)	0.9
Platelets, median x 10^9/L (range)	49 (21-155)	48 (3-279)	0.9
BM blast %, median (range)	76 (38-94)	76 (20-98)	0.9
t-AML, no. (%)	5 (25)	64 (42)	0.2
***RAS*, no. (%)**	5/18 (28)	24/85 (28)	0.9
***FLT3*, no. (%)**	4/18 (22)	10/92 (11)	0.2
***TP53*, no. (%)**	0/6 (0)	2/37 (5)	0.9
≥1 mutations, no. (%)	8/18 (44)	44/99 (44)	0.9
≥2 mutations, no. (%)	1/18 (6)	7/99 (7)	0.9
t(9;11), no. (%)	8 (40)	89 (59)	0.2
t(6;11), no. (%)	3 (15)	16 (11)	0.5
t(11;19), no. (%)	5 (24)	29 (19)	0.6
t(11;v)(q23;v), no. (%)	5 (25)	29 (19)	0.6
Extra-medullary disease, no. (%)	7 (35)	54 (36)	0.9
Monocytic phenotype, no. (%)	14 (70)	102 (67)	0.9

Values are n (%).
WBC white blood cell; BM, bone marrow; LDH, lactate dehydrogenase; t-aml; therapy related AML; values indicate mutated/tested genes. Extramedullary disease at diagnosis.
P: Kruskal-Wallis or Fisher exact test.