

Hypomethylating agents plus venetoclax *versus* intensive chemotherapy in acute myeloid leukemia with chromosome 5 and 7 abnormalities

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Supplemental Table 1: Distribution of patients by center.

Center	N (%)
Memorial Sloan Kettering Cancer Center	66 / 246 (27)
Dana-Farber Cancer Institute	98 / 246 (40)
Yale Cancer Center	21 / 246 (8)
Institut Paoli-Calmettes	32 / 246 (13)
Vilnius University Hospital Santaros Klinikos	29 / 246 (12)

Supplemental Table 2: Mutational alterations evaluated.

ASXL1	FLT3	PHF6
ATM	GATA1	PPM1D
BCOR	GATA2	PRPF8
BCORL1	GNAS	PTPN11
BRAF	GNB1	RAD21
BRCC3	IDH1	RIT1
BTK	IDH2	RUNX1
CALR	IKZF1	SETBP1
CBL	JAK1	SETD2
CDKN2A	JAK2	SF3B1
CEBPA	KIT	SH2B3
CREBBP	KRAS	SMC1A
CSF3R	MPL	SMC3
CTCF	MYC	SRSF2
CUX1	NF1	STAG2
DDX41	NFE2	TET2
DNMT3A	NOTCH1	TP53
EP300	NPM1	U2AF1
ETNK1	NRAS	WT1
ETV6	NSD2	XPO1
EZH2	PDS5B	ZRSR2

Supplemental Table 3: Baseline demographic and disease characteristics for patients age 60-75 with -7 and -5/del5q by overall group, IC treatment, and HMA+ven treatment.

	Overall (60-75) N=130	IC (60-75) N=42 (32%)	HMA+ven (60-75) N=88 (68%)	P-value
Chromosome 5 and 7 abnormalities, N (%)				
-5/del5q	60 / 130 (46)	22 / 42 (52)	38 / 88 (43)	0.29
-7	44 / 130 (34)	15 / 42 (36)	29 / 88 (33)	
Both -5/del5q and -7	26 / 130 (20)	5 / 42 (12)	21 / 88 (24)	
Patient and treatment characteristics				
Median age (range)	69 (60, 75)	66 (60, 74)	70 (60, 75)	<0.001
Male sex, N (%)	79 / 130 (61)	28 / 42 (67)	51 / 88 (58)	0.44
Prior myeloid malignancy, N (%)	42 / 130 (32)	16 / 42 (38)	26 / 88 (30)	0.42
Therapy-related, N (%)	38 / 130 (29)	10 / 42 (24)	28 / 88 (32)	0.41
Prior hypomethylating agent, N (%)	17 / 130 (13)	11 / 42 (26)	6 / 88 (7)	0.004
Concomitant cytogenetic and molecular abnormalities, N (%)				
Complex karyotype	94 / 130 (72)	27 / 42 (64)	67 / 88 (76)	0.21
Monosomal karyotype	91 / 130 (70)	26 / 42 (62)	65 / 88 (74)	0.22
Deletion 17p	36 / 130 (28)	8 / 42 (19)	28 / 88 (32)	0.15
<i>RAS</i> pathway	26 / 127 (20)	10 / 39 (26)	16 / 88 (18)	0.35
<i>ASXL1</i>	13 / 130 (10)	3 / 42 (7)	10 / 88 (11)	0.55
<i>DNMT3A</i>	24 / 130 (18)	7 / 42 (17)	17 / 88 (19)	0.81
<i>IDH 1 or 2</i>	14 / 130 (11)	6 / 42 (14)	8 / 88 (9)	0.38
<i>RUNX1</i>	17 / 130 (13)	10 / 42 (24)	7 / 88 (8)	0.023
<i>TET2</i>	17 / 130 (13)	3 / 42 (7)	14 / 88 (16)	0.27
Splicing factor mutation	21 / 126 (17)	10 / 38 (26)	11 / 88 (13)	0.070
Ontogeny as defined by co-occurring mutations, N (%)				
De novo	23 / 130 (18)	11 / 42 (26)	12 / 88 (14)	0.061
Secondary	30 / 130 (23)	12 / 42 (29)	18 / 88 (20)	
<i>TP53</i> mutated	77 / 130 (59)	19 / 42 (45)	58 / 88 (66)	

Supplemental Table 4: Treatment characteristics and rates of remission, MRD-negativity, and transplantation in patients age 60-75 with -7 and -5/del5q by overall group, IC treatment, and HMA+ven treatment.

	Overall (60-75) N=130	IC (60-75) N=42 (32%)	HMA+ven (60-75) N=88 (68%)	P-value
Treatment characteristics, N (%)	-	<u>7+3</u> : 23 / 42 (55) CPX-351: 19 / 42 (45)	<u>Aza/Ven</u> : 50 / 88 (57) <u>Dec/Ven</u> : 38 / 88 (43)	-
Clinical outcome, N (%)				
CR/CRi	50 / 106 (47)	17 / 39 (44)	33 / 67 (49)	0.69
MRD negativity	14 / 25 (56)	5 / 9 (56)	9 / 16 (56)	>0.99
Proceeded to transplant	43 / 130 (33)	20 / 42 (48)	23 / 88 (26)	0.018
30-day mortality	5 / 130 (4)	1 / 42 (2)	4 / 88 (5)	>0.99
60-day mortality	18 / 130 (14)	4 / 42 (10)	14 / 88 (16)	0.42

Supplemental Table 5: UVA of predictors of OS in patients with -7 and -5/del5q.

Characteristic	HR	95% CI	P-value
Both -5 or del(5q) and -7 vs. -5/del5q only	1.39	0.98, 1.97	0.068
-7 only vs. -5/del5q only	1.09	0.79, 1.52	0.6
Age at diagnosis	1.03	1.02, 1.05	<0.001
Prior myeloid malignancy	1.45	1.08, 1.94	0.014
Prior HMA	1.46	0.97, 2.19	0.070
Monosomal karyotype	1.68	1.21, 2.34	0.002
Complex karyotype	1.56	1.10, 2.20	0.012
Deletion 17p	0.89	0.65, 1.22	0.47
<i>TP53</i> mutation	1.52	1.14, 2.03	0.023
<i>BCOR</i> mutation (available in 235/246 patients)	0.43	0.18, 1.06	0.066
<i>KRAS</i> mutation	1.69	0.98, 2.92	0.059
<i>TET2</i> mutation	1.66	1.07, 2.58	0.023
Treatment with HMA+ven	1.63	1.21, 2.19	<0.001
Transplant (as a time-varying covariate)	0.31	0.21, 0.46	<0.001