

Supplementary Table 1. Baseline Molecular Abnormalities in all patients (n=66)

Mutation	N/total pts tested (%)	Mutation	N/total pts tested (%)	Mutation	N/total pts tested (%)
<i>TP53</i>	19/66 (29)	<i>KRAS</i>	5/66 (8)	<i>SETBP1</i>	3/66 (5)
<i>RUNX1</i>	14/66 (21)	<i>SF3B1</i>	5/66 (8)	<i>U2AF1</i>	3/66 (5)
<i>DNMT3A</i>	11/66 (17)	<i>SRSF2</i>	5/66 (8)	<i>ZRSR2</i>	3/66 (5)
<i>NRAS</i>	11/66 (17)	<i>TET2</i>	5/66 (8)	<i>CBL</i>	2/66 (3)
<i>ASXL1</i>	7/66 (11)	<i>ETV6</i>	4/66 (6)	<i>IRF1</i>	2/66 (3)
<i>NPM1</i>	7/66 (11)	<i>PTPN11</i>	4/66 (6)	<i>NF1</i>	2/66 (3)
<i>FLT3 ITD</i>	5/66 (8)	<i>WT1</i>	4/66 (6)	<i>SDHD</i>	2/66 (3)
<i>GATA2</i>	5/66 (8)	<i>BCORL1</i>	3/66 (5)	<i>STAG2</i>	2/66 (3)
<i>IDH1</i>	5/66 (8)	<i>EZH2</i>	3/66 (5)	<i>UTAF1</i>	2/66 (3)
<i>JAK2</i>	5/66 (8)	<i>IDH2</i>	3/66 (5)		

Supplementary Table 2. Disposition of patients after completing 1 cycle of therapy with CPX-351

Outcome of C1	Consolidation with CPX-351 N (%)	AlloHSCT Alone N (%)	Consolidation + AlloHSCT N (%)				
CR/Cri/MLFS	20 (30)	2 (3)	22 (33)				

Outcome of C1	Second Induction with CPX-351 N (%)	Allogeneic HSCT with CPX-351 N (%)	Allogeneic HSCT N (%)	CLAG-M N (%)	HiDAC N (%)	FLAG N (%)	HMA/ven N (%)
Refractory Disease	7 (32)	0 (0)	7 (32)	7 (11)	1 (2)	3 (5)	8 (12)

Abbreviations: CR= complete remission; Cri= complete remission with incomplete count recovery. MLFS= morphologic leukemia free state; Allo= allogeneic; HSCT=hematopoietic stem cell transplant; HMA= hypomethylating agent; Ven= venetoclax; CLAG-M= cladribine, cytarabine, mitoxantrone, GCSF; HiDAC= high dose cytarabine; FLAG= fludarabine, cytarabine, GCSF; C1= cycle 1

Supplementary Table 3. Outcomes by Subgroup Analysis

Response to Therapy	Entire Cohort (N=62)	TP53 mut (N=19)	TP53 WT (N=41)	HMA Naïve (N=46)	Prior HMA (N=16)
Pt Number (%)	N (%)	N (%)	N (%)	N (%)	N (%)
CR/CRI	27 (43.5%)	6 (31.5%)	21 (48.8%)	23 (50%)	4 (25%)
MLFS	2 (3.2%)	1 (5.2%)	1 (2.3%)	1 (2%)	1 (6.3%)
NR	33 (53%)	12 (63.2%)	19 (46.3%)	22 (47.8%)	11 (68.6%)
Median OS (Range in mos)	12.2 mos (0.2-36.2)	13.6 mos (0.6-28.3)	8.6 mos (0.2-36.2)	10.2 mos (0.5-28.5)	12.2 mos (1.3-36.2)
Event-free survival (Range in mos)	Not Reached (0.5-14.2)	Not Reached (0.5-13.7)	Not Reached (0.7-13)	Not Reached (0.5-13.7)	Not Reached (0.7-13.7)
	Entire Cohort (N=31)	TP53 mut (N=8)	TP53WT (N=21)	HMA Naïve (N=8)	Prior HMA (N=8)
Median OS landmark for HSCT (Range in mos)	Not Reached (0.5-14.2)	Not Reached (2.3-24.1)	Not Reached (0.1-34.1)	Not Reached (2.7-34.1)	15.95 (2.1-33.6)

Abbreviations: CR= complete remission; CRI= complete remission with incomplete count recovery; MLFS= morphologic leukemia free state; NR = no response; OS= overall survival; HSCT= hematopoietic stem cell transplant; WT= wildtype; HMA= hypomethylating agent; mos= months; mut = mutant

Supplementary Table 4. Median time to count recovery

	ANC (>500)	Platelet (>50K)
Median days (range)	37.2 (26 – 48)	39.8 (38 – 52)

Supplementary Table 5. Most commonly reported adverse events grade ≥ 3 in all patients (n=66)

	Neutropenic Fever	Sepsis	Pneumonia	Hemorrhage	Bacteremia	Progressive Disease
Grade ≥ 3 Events N (%)	29 (67)	14 (33)	11 (26)	4 (9)	8 (19)	0 (0)
Grade 5 Events N (%)	0 (0)	2 (3)	2 (3)	0 (0)	0 (0)	7 (11)