

Supplemental Table and Figures

Table S1 Correlation of EZH2 and PIK3IP1 expression with clinical features in AML cohort

| Characteristics | EZH2 Expression (N=88) | | p Value | PIK3IP1 Expression (N=88) | | p Value |
|---|------------------------|-----------------|--------------|---------------------------|-------------------|------------------|
| | High(n=22) | Low(n=66) | | High(n=66) | Low(n=22) | |
| Gender, n (%) | | | | | | |
| Male | 11 (50.0%) | 28 (42.4%) | 0.536 | 30 (45.5%) | 9 (40.9%) | 0.710 |
| Age, median (range), y | 66 (24-88) | 55 (18-82) | 0.033 | 61 (18-88) | 58 (24-88) | 0.855 |
| FAB subtype of AML, n (%) | | | 0.258 | | | 0.791 |
| M0 | 1 (4.5%) | 1 (1.5%) | | 1 (1.5%) | 1 (4.5%) | |
| M1 | 2 (9.1%) | 5 (7.6%) | | 5 (7.6%) | 2 (9.1%) | |
| M2 | 13 (59.1%) | 28 (42.4%) | | 33 (50.0%) | 8 (36.4%) | |
| M3 | 0 (0.0%) | 4 (6.1%) | | 2 (3.0%) | 2 (9.1%) | |
| M4 | 1 (4.5%) | 6 (9.1%) | | 5 (7.6%) | 2 (9.1%) | |
| M5 | 4 (18.2%) | 22 (33.3%) | | 19 (28.8%) | 7 (31.8%) | |
| M7 | 1 (4.5%) | 0 (0.0%) | | 1 (1.5%) | 0 (0.0%) | |
| WBC (x10⁹/L), median(range) | 7.5 (0.34-58.54) | 13 (0.37-201.9) | 0.088 | 8 (0.34-201.9) | 15 (0.37-179.7) | 0.099 |
| Hb (g/L), median(range) | 71 (37-118) | 77.5 (31-123) | 0.700 | 75 (31-120) | 82.5 (36-123) | 0.182 |
| PLT (x10⁹/L), median(range) | 22.5 (5-265) | 42.5 (3-252) | 0.047 | 38.5 (3-265) | 39 (14-252) | 0.795 |
| BM blasts (%), median (range) | 51 (4-96) | 60.4 (17-97.6) | 0.221 | 58.6 (17-96) | 56 (4.80-97.6) | 0.658 |
| Cytogenetics, n (%) | | | | | | |
| Normal | 9 (47.4%) | 36 (58.1%) | 0.444 | 34 (45.0%) | 11 (55.0%) | 1.000 |
| Complex Karyotype | 5 (26.3%) | 7 (11.5%) | 0.114 | 10 (16.7%) | 2 (10.0%) | 0.470 |
| 7q-/7 | 3 (15.8%) | 1 (1.6%) | 0.013 | 2 (3.3%) | 2 (10.0%) | 0.236 |
| Gene mutations, n (%) | | | | | | |
| TP53 | 3 (13.6%) | 3 (4.5%) | 0.143 | 1 (1.5%) | 5 (22.7%) | 0.001 |
| ASXL1 | 2 (9.1%) | 2 (3.0%) | 0.237 | 3 (4.5%) | 1 (4.5%) | 1.000 |
| DNMT3A | 2 (9.1%) | 15 (22.7%) | 0.161 | 4 (6.1%) | 13 (59.1%) | <0.001 |
| NPM1 | 1 (4.5%) | 15(22.7%) | 0.056 | 7 (10.6%) | 9 (40.9%) | 0.001 |
| KRAS | 0 (0.0%) | 2 (3.0%) | 0.409 | 1 (1.5%) | 1 (4.5%) | 0.440 |
| NRAS | 1 (4.5%) | 4 (6.1%) | 0.790 | 3 (4.5%) | 2 (9.1%) | 0.425 |
| FLT3-ITD | 0 (0.0%) | 8 (12.1%) | 0.087 | 5 (7.6%) | 2 (9.1%) | 0.820 |
| Complete response, n (%) | 13 (59.1%) | 57 (86.4%) | 0.006 | 54 (81.8%) | 16 (72.7%) | 0.360 |
| Refractory/Relapse, n (%) | 9 (45.0%) | 14 (21.2%) | 0.035 | 15 (23.1%) | 8 (38.1%) | 0.176 |
| Median OS, months (95% CI) | 12.0 (1.71-22.29) | NR | 0.007 | 30.0 | 20.0 (7.05-32.95) | 0.500 |

WBC, white blood cells; Hb, hemoglobin; PLT, Platelet count; BM, bone marrow; Complex karyotype, defined as having 3 or more chromosomal abnormalities in the absence of one of the WHO–designated recurrent genetic abnormalities; OS, overall survival; SE, Standard error; CI, Confidence Interval; NR, not reached.

Table S2 Clinical Features of the patients in the AML cohort

| Patient ID | FAB subtype | Gender | Age | WBC(10 ⁹ /L) | Hb(g/L) | PLT(10 ⁹ /L) | BM Blasts | Molecular features | Cytogenetics | Treatment response | RFS(months) | Refractory/Relapse(yes/no) | OS(months) | Survival at last follow-up(alive/died) |
|------------|-------------|--------|-----|-------------------------|---------|-------------------------|-----------|----------------------------|--|--------------------|-------------|----------------------------|------------|--|
| AML_1 | M2 | Female | 88 | 6.13 | 71 | 74 | 34.00% | negative | Normal | NR | | no | 5 | died |
| AML_2 | M2 | Female | 70 | 57.06 | 80 | 21 | 34.80% | negative | t(9,22) | NR | | yes | 12 | died |
| AML_3 | M4 | Female | 35 | 30.67 | 123 | 62 | 68.40% | CBFβ/MYH11 | 46,XX,inv(16)(p13q22)/(20) | CR | 29 | no | 30 | alive |
| AML_4 | | | | | | | | | 46,XX,t(8;21)(q22;q22)[1]/46,Idem,del(9)(q22)[1]/45,Idem,-X,del(9)(q22)[3]/46,XX[15] | CR | 53 | no | 54 | alive |
| AML_5 | M2 | Female | 62 | 2.73 | 80 | 46 | 63.20% | AML1/ETO | FLT3-ITD, | CR | | | | |
| AML_5 | M2 | Female | 49 | 20.47 | 76 | 33 | 40.40% | NPM1 | Normal | NR | 38 | no | 42 | alive |
| AML_6 | M5 | Female | 55 | 6.58 | 65 | 102 | 31.20% | NPM1, CEBPA | Normal | CR | 6 | no | 5 | alive |
| AML_7 | M5 | Female | 54 | 44.98 | 121 | 116 | 61.60% | DNMT3A | Normal | CR | 60 | no | 61 | alive |
| AML_8 | | | | | | | | HOX11 rearrangement, NPM1, | | | | | | |
| AML_8 | M5 | Female | 81 | 44.24 | 102 | 79 | 60% | DNMT3A | Normal | NR | 10 | yes | 16 | died |
| AML_9 | M4 | Female | 56 | 47.7 | 65 | 25 | 53.20% | FLT3-ITD | Normal | CR | 29 | yes | 36 | alive |
| AML_10 | M1 | Male | 49 | 179.7 | 99 | 63 | 97.60% | FLT3-ITD, NPM1 | Normal | PR | 11 | no | 15 | died |
| AML_11 | M5 | Female | 61 | 58.54 | 100 | 22 | 59.20% | negative | Normal | CR | 1 | no | 1 | alive |
| AML_12 | M3 | Female | 45 | 0.37 | 63 | 20 | 61.20% | PML/RARα | t(15,17) | CR | | no | 52 | alive |
| AML_13 | M2 | Male | 68 | 3.92 | 86 | 265 | 31.20% | IDH2 | 46,XY,del(7)(q31)[12]/46,XY[5] | PR | 2 | no | 6 | alive |
| AML_14 | M2 | Male | 48 | 18.24 | 87 | 18 | 46% | HOX11/EVI1, NPM1 | Normal | CR | 21 | yes | 32 | alive |
| AML_15 | M2 | Female | 41 | 122.12 | 49 | 18 | 62.40% | FLT3-ITD | 46,XX,del(20)(q13)[20] | NR | | yes | 2 | alive |
| AML_16 | M5 | Female | 48 | 32.81 | 109 | 37 | 85.60% | CBFβ/MYH11 | 46, XX, ? add(7)(q11.2), inv(16)(p13q22)[20] | CR | 46 | no | 47 | alive |
| AML_17 | M5 | Female | 82 | 11.62 | 107 | 10 | 65.60% | CEBPA | Normal | PR | 1 | no | 1 | alive |
| AML_18 | M2 | Male | 75 | 201.9 | 96 | 36 | 89% | negative | Normal | PR | | yes | 2 | died |
| AML_19 | M5b | Female | 73 | 108.15 | 95 | 42 | 65.60% | FLT3-ITD, NPM1 | Normal | NR | 1 | yes | 1 | died |
| AML_20 | M0 | Male | 55 | 25.66 | 82 | 31 | 76% | RUNX1 | Normal | PR | 2 | no | 2 | alive |
| AML_21 | M2 | Female | 88 | 8.47 | 81 | 14 | 24% | negative | Normal | PR | 1 | no | 3 | died |
| AML_22 | M2 | Male | 64 | 2.99 | 83 | 63 | 26% | negative | 47, XY, +1, der(1;19)(q10;q10),+19[19]/46,XY[1] | NR | 7 | no | 8 | died |
| AML_23 | M4 | Female | 44 | 132.28 | 82 | 37 | 54.80% | FLT3-ITD | Normal | CR | 1 | no | 2 | alive |
| AML_24 | M3 | Female | 25 | 0.8 | 74 | 93 | 55.20% | | 47, XX, +8, t(15;17)(q22;q21)[14]/46,XX[6] | CR | | no | 27 | alive |
| AML_25 | M3 | Female | 50 | 52.67 | 71 | 82 | 93.30% | PML-RARα | t(15,17) | CR | 17 | no | 18 | alive |
| AML_26 | M5 | Male | 75 | 39.54 | 57 | 39 | 36.40% | SRSF2 | 46,XY,del(20)(q11)[11]/47,idem,+8[9] | CR | 2 | no | 2 | died |
| AML_27 | M5 | Female | 69 | 52.02 | 100 | 159 | 65.60% | DNMT3A, TET2 | Normal | CR | 11 | no | 12 | died |
| AML_28 | M1 | Male | 56 | 52.16 | 72 | 23 | 90.40% | negative | 46, XY, add(21)(p11) [6]/46,XY[14] | CR | 18 | yes | 16 | died |
| AML_29 | M4 | Male | 25 | 47.48 | 72 | 50 | 49.20% | CBFβ/MYH11 | 46,XY,inv(16)(p13q22)[20] | CR | 37 | no | 38 | alive |
| AML_30 | M5 | Male | 67 | 0.86 | 56 | 26 | 33.20% | ASXL1, BCOR | Normal | NR | 1 | no | 2 | alive |
| | | | | | | | | IDH, RUNX1 | | | | | | |

Table S2 Clinical Features of the patients in the AML cohort (continue1)

| Patient ID | FAB subtype | Gender | Age | WBC(10Hb(g/PLT(10 ⁹ / ⁹ L/L) | | | BM Blasts | Molecular features | Cytogenetics | Treatment response | RFS(months) | Refractory/Relapse(yes/no) | OS(months) | Survival at last follow-up(alive/died) |
|------------|-------------|--------|-----|--|-----|----|-----------|---------------------------|---|--------------------|-------------|----------------------------|------------|--|
| AML_31 | M0 | Female | 60 | 35.48 | 53 | 15 | 48.80% | CBFβ/MYH11, NRAS | t(8,10); inv(16) | CR | 4 | no | 5 | alive |
| AML_32 | M2 | Male | 67 | 2.35 | 99 | 51 | 62.80% | TET2 | Normal | CR | 25 | yes | 30 | died |
| AML_33 | M2 | Male | 42 | 154.9 | 82 | 33 | 72.80% | FLT3, CBFβ/MYH11 | 46,XY,inv(16)(p13q22)[3]/47,idem,+22[15]/46,XY[2] | CR | 13 | no | 14 | died |
| AML_34 | M2 | Female | 55 | 7.23 | 83 | 62 | 54.80% | TET2, STAG2, CEBPA | Normal | CR | 38 | no | 39 | alive |
| AML_35 | M2 | Male | 78 | 0.34 | 69 | 20 | 75.60% | RUNX1, SF3B1 | No mitotic phase | NR | | | 1 | died |
| AML_36 | M2 | Female | 62 | 1.8 | 118 | 79 | 30.88% | WT1 high expression | Normal | CR | 17 | yes | 26 | died |
| AML_37 | M2 | Male | 24 | 4.41 | 65 | 5 | 77.60% | AML1/ETO | No mitotic phase | CR | 2 | no | 3 | alive |
| AML_38 | M2 | Female | 75 | 15.17 | 90 | 23 | 22.60% | AML1/ETO | 45, X,-X,t (8 ; 21) (q22 ; q22) [20] | CR | 14 | yes | 92 | alive |
| AML_39 | M2 | Female | 40 | 13.6 | 44 | 17 | 70.80% | GATA2 | No mitotic phase | CR | 1 | yes | 30 | died |
| AML_40 | M2 | Female | 66 | 3.29 | 61 | 19 | 27.50% | negative KIT, | Normal | CR | 2 | no | 3 | died |
| AML_41 | M2 | Male | 44 | 33.13 | 68 | 15 | 75.60% | AML1/ETO | Normal | CR | 5 | no | 6 | alive |
| AML_42 | M2 | Female | 35 | 10.37 | 82 | 24 | 32.80% | AML1/ETO | 46, XX, t(8 ; 21) (q22 ; q22) [10] | CR | 8 | yes | 15 | died |
| AML_43 | M2 | Male | 67 | 12.43 | 70 | 23 | 53.20% | TET2 | Normal | PR | | yes | 13 | died |
| AML_44 | M2 | Female | 24 | 26.66 | 36 | 23 | 55.20% | WT1 high expression | 46,XX,?del(9)(q22)[9]/46,XX[11] | CR | 33 | no | 34 | alive |
| AML_45 | M3 | Female | 54 | 0.87 | 67 | 85 | 69.5% | PML/RARα | t (15,17) | CR | 17 | no | 18 | alive |
| AML_46 | M5b | Female | 53 | 69.32 | 53 | 30 | 46.80% | TET2, WT1, KRAS | Normal | CR | 18 | no | 20 | died |
| AML_47 | M2 | Female | 50 | 1.08 | 89 | 45 | 63.50% | IDH2, CEBPA | No mitotic phase | CR | 14 | yes | 34 | alive |
| AML_48 | M2 | Female | 48 | 14.43 | 31 | 3 | 60.80% | AML1/ETO, KIT | 46,XX,inv(8)(p23q21),t(8;21)(q22;q22)[11]/47,idem,+4[4] | CR | 13 | no | 14 | alive |
| AML_49 | M4 | Female | 43 | 62.12 | 81 | 43 | 75.50% | CBFβ/MYH11, KIT, FLT3 | 47,XX,inv(16)(p13q21),+22[20] | CR | 18 | no | 19 | alive |
| AML_50 | M5 | Female | 34 | 0.81 | 64 | 25 | 87.60% | U2AF1, SETBP1 | 46,X,del(X)(q24),t(9;11)(p22;q23),?add(17)(q25) | NR | 22 | no | 27 | alive |
| AML_51 | M2 | Female | 48 | 2.19 | 89 | 78 | 17% | IDH1, TET2 | No mitotic phase | CR | 19 | no | 20 | alive |
| AML_52 | M2 | Male | 43 | 1.6 | 62 | 43 | 23% | RUNX1, U2AF1, BCOR | Normal | CR | 8 | no | 15 | died |
| AML_53 | M2 | Female | 21 | 6.72 | 68 | 18 | 44% | GATA2, CEBPA | Normal | CR | 18 | no | 19 | alive |
| AML_54 | M5 | Male | 79 | 4.12 | 78 | 54 | 46.40% | TET2, DNMT3A | Normal | CR | 4 | no | 6 | died |
| AML_55 | M2 | Male | 72 | 2.37 | 72 | 86 | 63.20% | TET2 | Normal | CR | 15 | no | 18 | died |
| AML_56 | M1 | Female | 75 | 47.99 | 71 | 53 | 54.40% | DNMT3A, TET2 | Normal | NR | 5 | yes | 5 | died |
| AML_57 | M7 | Male | 65 | 5.4 | 64 | 70 | 34.80% | TP53 | Complex Karyotype | PR | - | yes | 1 | died |
| AML_58 | M5b | Male | 54 | 36.11 | 120 | 62 | 52% | KRAS | Normal | CR | 16 | no | 17 | alive |
| AML_59 | M5 | Female | 66 | 1.39 | 66 | 24 | 58% | DNMT3A, IKZF1, IDH2, BCOR | Normal | CR | 5 | no | 6 | alive |
| AML_60 | M2 | Male | 78 | 4.21 | 89 | 15 | 64.80% | ASXL1, IDH2, RUNX1, PHF6 | Normal | PR | | yes | 3 | died |

Table S2 Clinical Features of the patients in the AML cohort (continue2)

| Patient ID | FAB subtype | Gender | Age | WBC(10 ⁹ Hb(g/ ⁹ L)/L) | PLT(10 ⁹ BM Blasts | Molecular features | Cytogenetics | Treatment response | RFS(months) | Refractory/Relapse(yes/no) | OS(months) | Survival at last follow-up(alive/died) | |
|------------|-------------|--------|-----|--|-------------------------------|--------------------|--|--|-------------|----------------------------|------------|--|-------|
| AML_61 | M2 | Female | 75 | 11.43 | 95 | 43 77.00% | TP53, IDH2 | 43~45,X,-X,idic(11)(p11),-14,-15,-16,-17,-18,+4~6mar,inc[cp6]/46,XX[5] ; FISH:7q-/7 : 3%,+8 : 9%,17p- : 94.5% , -17 : 18.7%, | NR | | | | |
| AML_62 | M4 | Male | 48 | 6.63 | 37 | 11 23.50% | ZRSR2 | 46, XY,inv (3) (q21q26)[6]/46,XY[4] | PR | 9 | yes | 15 | alive |
| AML_63 | M2 | Male | 59 | 7.98 | 54 | 21 67.20% | KIT, ASXL1, AML1/ETO | 46, XY, t (8 ; 21) (q22 ; q22)[20] | CR | 2 | no | 4 | died |
| AML_64 | M1 | Male | 47 | 23.36 | 85 | 67 96% | IDH1, FLT3, TP53 | Normal | CR | 2 | no | 3 | alive |
| AML_65 | M5 | Female | 64 | 1.22 | 61 | 20 40.00% | TP53, PTPN11, ASXL2 | 46, XXdel(1)(p11p12),del(5)(q13q33)+8,add(9)(q34),+11,der(17;20)(q10;p10),-18[20] | NR | 1 | yes | 6 | alive |
| AML_66 | M5a | Female | 70 | 25.98 | 79 | 88 85.20% | PTPN11, MLL/AF9 | 47, XX,+8[20] | CR | 4 | no | 24 | alive |
| AML_67 | M4 | Male | 41 | 9.59 | 66 | 36 53.60% | CSF3R, WT1, CBFβ/MYH11 | Normal | CR | 23 | no | 24 | alive |
| AML_68 | M2 | Male | 48 | 10.6 | 77 | 23 63.20% | DNMT3A | Normal | CR | 2 | no | 5 | died |
| AML_69 | M5 | Male | 57 | 4.8 | 75 | 67 24.40% | TP53 | 43-48, XY,+X,psu dic(5;3)(q35;p21),-7,add(11)(q13),-12,-13,add(17)(p13),+2~3mar[20] | CR | 6 | no | 7 | died |
| AML_70 | M1 | Female | 70 | 7.68 | 97 | 12 89% | WT1 | Normal | CR | 15 | no | 17 | alive |
| AML_71 | M5 | Female | 18 | 0.4 | 36 | 25 54.40% | negative | No mitotic phase | CR | 26 | no | 28 | alive |
| AML_72 | M2 | Male | 73 | 0.69 | 42 | 29 34.80% | ETV6 | 46,XY[20], 17p- 6.5% | CR | 21 | no | 22 | alive |
| AML_73 | M5 | Male | 78 | 73.87 | 91 | 90 49.60% | DNMT3A, TET2, NPM1 | Normal | CR | 3 | no | 6 | died |
| AML_74 | M2 | Male | 74 | 8.28 | 119 | 66 53.20% | DNMT3A, CEBPA | Normal | CR | 11 | no | 12 | alive |
| AML_75 | M2 | Male | 71 | 5.61 | 84 | 105 56.80% | DNMT3A, TET2, NPM1, FLT3-ITD | No mitotic phase | CR | 7 | no | 8 | died |
| AML_76 | M1 | Male | 73 | 7.71 | 68 | 50 92.80% | TET2, DNMT3A, NPM1 | Normal | CR | 16 | no | 17 | alive |
| AML_77 | M2b | Female | 26 | 33.55 | 56 | 37 48.80% | AML1/ETO, PTEN, ASXL1, CSF3R | 46,XX, t (8 ; 21) (q22 ; q22)[19]/46,XX[1], RUNX1/RUNX1T1+:99% | CR | 2 | no | 3 | alive |
| AML_78 | M5 | Male | 70 | 10.2 | 101 | 252 44% | DNMT3A, NPM1, IDH1, NRAS | Normal | CR | 1 | no | 2 | died |
| AML_79 | M2 | Female | 69 | 7.79 | 55 | 121 20.40% | RAD21, AML1/ETO | 45,X,t (8 ; 21) (q22 : q22)[17]/46,XX[3] | CR | 6 | no | 7 | alive |
| AML_80 | M1 | Female | 75 | 5.12 | 75 | 21 81.00% | DNMT3A, TET2CEBPA:NM_004364.4: exon1:c.1042_1043dupCT:p.Ser348ArgfsTer75 38.78% 移码突变 ; CEBPA: NM_004364.4:exon1:c.484C>T:p.Q162X 38.85% 无义突变 ; WT1/ABL1 0.250% ; | 46, XX,del(11)(q14)[12]/47,idem,+?8[2]/46,XX[2] | CR | 1 | no | 2 | alive |
| AML_81 | M5b | Male | 64 | 20.66 | 58 | 28 27.60% | SF3B1, FLT3-ITD, RUNX1 | Normal | CR | 17 | no | 18 | alive |
| AML_82 | M2 | Female | 64 | 1.71 | 92 | 109 62.00% | NPM1, IDH1, DNMT3A | Normal | CR | 2 | no | 3 | alive |
| AML_83 | M5b | Female | 73 | 101.82 | 109 | 38 76.31% | TET2, GATA1, NRAS, NPM1 | 46, XX, +1, psu dic(4;1)(p16;p11)[9]/46,XX[1] | NR | | yes | 2 | alive |
| AML_84 | M2 | Male | 63 | 1.54 | 62 | 99 76.00% | TET2, DNMT3A, NPM1 | Normal | CR | 10 | no | 11 | alive |
| AML_85 | M2 | Male | 71 | 6.38 | 60 | 54 48.00% | TP53 | 42,X,-Y,t(2;2)(p24;p13),del(3)(q26.2),inv(4)(p16q12),del(5)(q23),+11,der(11;14)(q10;q10),-17,-18,del(20)(q12),-21[20] | CR | 4 | no | 6 | died |
| AML_86 | M5b | Male | 59 | 95.6 | 78 | 68 80.40% | DNMT3A, NPM1, IDH2, NRAS | Normal | CR | 9 | no | 10 | alive |
| AML_87 | M5b | Female | 53 | 11.88 | 97 | 85 77.00% | CBL, NPM1 | No mitotic phase | CR | 3 | yes | 8 | alive |
| AML_88 | M5a | Male | 69 | 9.25 | 116 | 140 96.00% | WT1 high expression | 47~48, XY, del(1)(q32), del(5)(q15q31),-7,add(9)(p13),-12,+19,-22,+2~3mar[cp4]/46,XY ,del(5)(q15q31),-7,-19,-22,+mar1,+mar2,+mar3[3]/46XY [13] 。 5q-:65%,7q-/7 94% | PR | | yes | 4 | died |

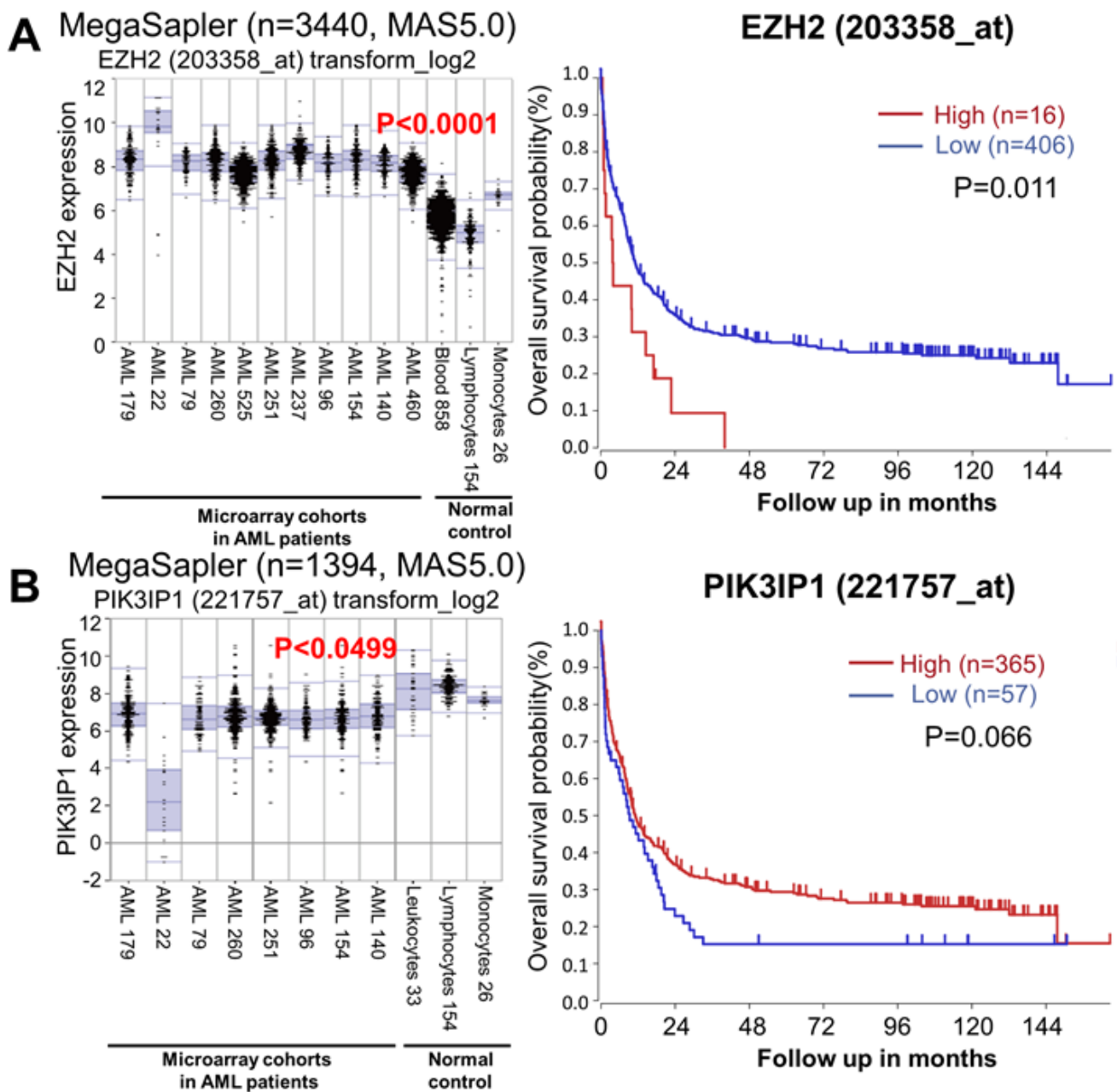


Figure S1. Expression of EZH2 or PIK3IP1 in blood or bone marrow samples of AML patients Versus normal controls from MegaSapler dataset and their association with survival. (A, B) The mRNA level of EZH2 is upregulated (A, left panel) while PIK3IP1 is downregulated (B, left panel) in AML cohorts compared to that of normal control. Association of EZH2^{lower} or PIK3IP1^{higher} with a longer OS compared to EZH2^{Higher} or PIK3IP1^{Lower} (A & B, right panel).

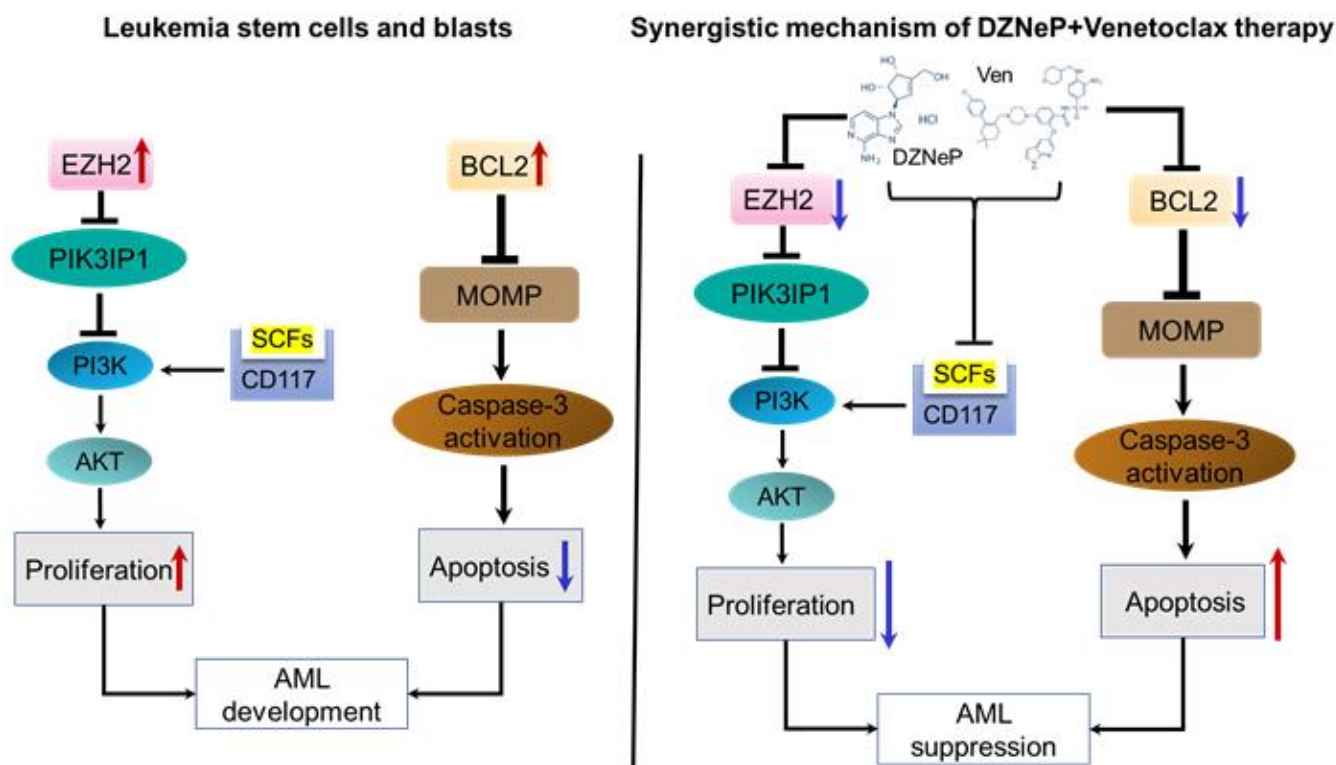


Figure S2. Mechanism model for the synergistic anti-leukemic effect of DZNeP+Ven in AML. In leukemia cells, highly expressed EZH2 and BCL2 promote the proliferation of AML cells and suppress apoptosis through activation of PI3K/AKT signaling. CD117 (c-KIT) is also activated through PI3K/AKT signaling. DZNeP treatment increases the expression of PIK3IP1, the PI3K/AKT signaling suppressor, which causes a significant proliferation arrest; and Ven induces apoptosis through promoting MOMP. Combination treatment of DZNeP+Ven shows the synergistic effects of proliferation arrest and apoptosis through enhancing expression of PIK3IP1 and decreasing c-KIT in AML. (Abbreviation: SCFs, stem cell factors; MOMP, mitochondrial outer membrane permeabilization)