**Prognostic Significance of the European LeukemiaNet Standardized System for Reporting Cytogenetic and Molecular Alterations in Acute Myeloid Leukemia: a Study of 1,550 Adults With Primary Disease**

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## DATA SUPPLEMENT

## METHODS

### *Treatment protocols*

Younger (aged <60 years) patients enrolled onto Cancer and Leukemia Group B (CALGB) 19808 (n=486) were randomly assigned to receive induction chemotherapy with cytarabine, daunorubicin, and etoposide with or without a multidrug resistance protein inhibitor valspodar. Upon attainment of complete remission (CR), patients with core-binding factor (CBF) acute myeloid leukemia (AML) were assigned to receive postremission therapy containing three courses of high-dose cytarabine (HiDAC). Patients with non-CBF AML were assigned to intensification with HiDAC and etoposide for stem-cell mobilization followed by myeloablative treatment with busulfan and etoposide supported by autologous peripheral blood stem-cell transplantation.[1] Patients enrolled onto CALGB 9621 (n=250) were treated similarly to those on CALGB 19808, as previously reported.[2] Patients enrolled onto CALGB 8525 (n=178) received induction chemotherapy consisting of cytarabine in combination with daunorubicin, and were randomly assigned to consolidation with different doses of cytarabine followed by maintenance treatment.[3] Patients enrolled onto CALGB 8923 (n=122) received induction chemotherapy consisting of cytarabine and daunorubicin and were randomly assigned to receive postremission therapy with cytarabine alone or in combination with mitoxantrone.[4] Patients enrolled onto 9720 (n=288) and CALGB 9420 (n=39) received induction chemotherapy consisting of cytarabine in combination with daunorubicin and etoposide, with (CALGB 9420) or with/without (CALGB 9720) valspodar.[5-7] The valspodar arm of CALGB 9720 was closed after random assignment of 120 patients

because of excessive early deaths, and enrollment continued on the chemotherapy-only control arm. Patients enrolled onto CALGB 9420 received postremission therapy with HiDAC (2 g/m$^2$/d) alone, and patients on CALGB 9720 received a single cytarabine/daunorubicin consolidation course and then were randomly assigned to low-dose recombinant interleukin-2 maintenance therapy or none.[5,6] Patients enrolled onto CALGB 10201 (n=187) received induction chemotherapy consisting of cytarabine and daunorubicin, with or without the *BCL2* antisense oblimersen sodium. The consolidation regimen included two cycles of cytarabine (2 g/m$^2$/d) with or without oblimersen.[8] None of the protocols included allogeneic stem cell transplantation in first CR.

***Definition of clinical endpoints***

Clinical endpoints were defined according to generally accepted criteria.[9] Per protocol, all patients were to receive at least one induction cycle. For patients with residual leukemia present in a bone marrow biopsy after one induction cycle, a second cycle of induction was administered. CR required a bone marrow (BM) aspirate with cellularity >20% with maturation of all cell lines, <5% blasts and undetectable Auer rods; in peripheral blood, an absolute neutrophil count of ≥1.5 x $10^9$/L, platelet count of >100 x $10^9$/L, and leukemic blasts absent; and no evidence of extramedullary leukemia, all of which had to persist for ≥4 weeks.[9] Relapse was defined by the presence of ≥5% BM blasts, or circulating leukemic blasts, or the development of extramedullary leukemia. Disease-free survival (DFS) was measured from the date of CR until the date of relapse or death (from any cause); patients alive and in CR were censored at last follow-up. Overall survival (OS) was measured from the date of study entry until the date of death (from any cause); patients alive at last follow-up were censored.

***Statistical analyses***

Baseline characteristics for continuous variables were compared using the Wilcoxon rank-sum test for two groups and the Kruskal-Wallis test for more than two groups.

Multivariable logistic regression models were generated for attainment of CR, and multivariable proportional hazards models were constructed for DFS and OS, using a limited backwards elimination procedure. Variables considered for model inclusion and

evaluated in univariable models were: European LeukemiaNet (ELN) Genetic Groups,[10] age (as a continuous variable, in 10-year increments), sex (male *v* female), race (white *v* nonwhite), white blood cell count (in 50-unit increments), hemoglobin (as a continuous variable), platelet count (in 50-unit increments), and extramedullary involvement (present *v* absent). Variables significant at $\alpha = .20$ from the univariable analyses were considered for multivariable analyses. For the time-to-event endpoints, the proportional hazards assumption was checked for each variable individually.

## SUPPLEMENTAL REFERENCES


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**Table A1**. Pretreatment Clinical Characteristics and Outcome of the Entire Cohort of 1,550 Patients With Primary Acute Myeloid Leukemia and of Younger (<60 Years) and Older (≥60 Years) Patients

| Characteristic | All Patients (n=1,550) | Younger Patients (n=818) | Older Patients (n=732) | *P** |
|---|---|---|---|---|
| Age, years | | | | <.001 |
| Median | 58 | 44 | 69 | |
| Range | 17-86 | 17-59 | 60-86 | |
| Male sex, no. (%) | 848 (55) | 429 (52) | 419 (57) | .06 |
| Race, no. (%) | | | | .003 |
| White | 1319 (86) | 667 (84) | 642 (89) | |
| Nonwhite | 210 (14) | 131 (16) | 79 (11) | |
| Hemoglobin, g/dL | | | | .13 |
| Median | 9.3 | 9.2 | 9.3 | |
| Range | 2.9-80.6 | 2.9-80.6 | 3.0-41.6 | |
| Platelets, $x10^9$/L | | | | .04 |
| Median | 56 | 53 | 60 | |
| Range | 4-989 | 4-513 | 4-989 | |
| WBC count, $x10^9$/L | | | | <.001 |
| Median | 13.8 | 17.5 | 9.2 | |
| Range | 0.4-450.0 | 0.4-295.0 | 0.6-450.0 | |
| Percentage of blood blasts | | | | <.001 |
| Median | 42 | 48 | 33 | |
| Range | 0-99 | 0-98 | 0-99 | |
| Percentage of bone marrow blasts | | | | .57 |
| Median | 61 | 62 | 60 | |
| Range | 1-99 | 1-98 | 4-99 | |
| FAB category, no. (%) | | | | <.001 |
| M0 | 56 (5) | 31 (5) | 25 (5) | |
| M1 | 233 (20) | 124 (19) | 109 (22) | |
| M2 | 381 (33) | 203 (30) | 178 (36) | |
| M4 | 306 (26) | 213 (32) | 93 (19) | |
| M5 | 145 (12) | 81 (12) | 64 (13) | |
| M6 | 38 (3) | 17 (3) | 21 (4) | |
| M7 | 3 (1) | 1 (1) | 2 (1) | |
| Extramedullary involvement, no. (%) | 340 (23) | 196 (25) | 144 (21) | .05 |
| Complete remission rate, no. (%) | 1078 (70) | 646 (79) | 431 (59) | <.001 |
| Disease-free survival† | | | | <.001 |
| Median, years | 1.0 | 1.3 | 0.7 | |
| Disease-free at 3 years, % (95% CI) | 29 (26-31) | 39 (35-43) | 13 (10-17) | |
| Overall survival‡ | | | | <.001 |
| Median, years | 1.3 | 2.0 | 0.8 | |
| Alive at 3 years, % (95% CI) | 30 (27-32) | 43 (40-47) | 14 (12-17) | |

Abbreviations: WBC, white blood cell; FAB, French-American-British classification.

* *P*-values pertain to comparisons between younger (<60 years) and older (≥60 years) patients. *P*-values for categorical variables are from Fisher's exact test and *P*-values for continuous variables are from the Wilcoxon rank-sum test.

† The median follow-up times for patients who have not had an event were 7.7 years (range, 0.6-19.1) for the entire patient cohort, 7.9 years (range, 0.6-19.1) for younger and 5.9 years (range, 4.4-16.4) for older patients.

‡ The median follow-up times for patients alive were 7.5 years (range, 0.6-19.1) for the entire patient cohort, 7.6 years (range, 0.6-19.1) for younger and 6.1 years (range, 2.3-16.4) for older patients.

**Table A2**. Pretreatment Clinical Characteristics of Younger Patients under the Age of 60 Years with Primary Acute Myeloid Leukemia Classified into the European LeukemiaNet Genetic Groups

| Characteristic | Favorable (n=339) | Intermediate-I (n=144) | Intermediate-II (n=156) | Adverse (n=179) | *P** |
|---|---|---|---|---|---|
| Age, years | | | | | .004 |
| Median | 42 | 46 | 44 | 45 | |
| Range | 17-59 | 18-59 | 17-59 | 17-58 | |
| Male sex, no. (%) | 179 (53) | 63 (44) | 83 (53) | 104 (58) | .08 |
| Race, no. (%) | | | | | .02 |
| White | 282 (84) | 129 (91) | 127 (82) | 139 (79) | |
| Nonwhite | 52 (16) | 13 (9) | 28 (18) | 38 (21) | |
| Hemoglobin, g/dL | | | | | .71 |
| Median | 9.3 | 9.2 | 9.2 | 9.2 | |
| Range | 4.0-12.3 | 4.6-25.1 | 2.9-15.1 | 4.2-13.8 | |
| Platelets, $x10^9$/L | | | | | <.001 |
| Median | 46 | 57 | 63 | 51 | |
| Range | 5-466 | 8-395 | 6-384 | 4-247 | |
| WBC count, $x10^9$/L | | | | | <.001 |
| Median | 20.1 | 27.0 | 15.0 | 7.5 | |
| Range | 0.4-295.0 | 0.8-161.5 | 0.7-276.8 | 0.6-225.3 | |
| Percentage of blood blasts | | | | | <.001 |
| Median | 50 | 60 | 46 | 32 | |
| Range | 0-97 | 0-91 | 0-98 | 0-91 | |
| Percentage of bone marrow blasts | | | | | <.001 |
| Median | 59 | 65 | 70 | 56 | |
| Range | 2-95 | 18-91 | 1-93 | 5-93 | |
| FAB category, no. (%) | | | | | <.001 |
| M0 | 0 (0) | 8 (7) | 7 (5) | 16 (12) | |
| M1 | 45 (16) | 31 (27) | 29 (22) | 19 (14) | |
| M2 | 102 (35) | 32 (28) | 30 (23) | 39 (29) | |
| M4 | 120 (41) | 31 (27) | 32 (25) | 30 (22) | |
| M5 | 20 (7) | 8 (7) | 32 (25) | 21 (16) | |
| M6 | 3 (1) | 5 (4) | 0 (0) | 9 (7) | |
| M7 | 0 (0) | 0 (0) | 0 (0) | 1 (1) | |
| Extramedullary involvement, no. (%) | 94 (28) | 36 (26) | 38 (26) | 28 (17) | .04 |

Abbreviations: WBC, white blood cell; FAB, French-American-British classification.

***** *P*-values for categorical variables are from Fisher's exact test, *P*-values for continuous variables are from the Kruskal-Wallis test.

**Table A3**. Pretreatment Clinical Characteristics of Patients Aged 60 Years and Older With Primary Acute Myeloid Leukemia Classified into the European LeukemiaNet Genetic Groups

| Characteristic | Favorable (n=145) | Intermediate-I (n=136) | Intermediate-II (n=222) | Adverse (n=229) | *P** |
|---|---|---|---|---|---|
| Age, years | | | | | .007 |
| Median | 67 | 70 | 69 | 69 | |
| Range | 60-81 | 60-83 | 60-86 | 60-85 | |
| Male sex, no. (%) | 68 (47) | 77 (57) | 140 (63) | 134 (59) | .02 |
| Race, no. (%) | | | | | .74 |
| White | 128 (90) | 123 (91) | 195 (89) | 196 (88) | |
| Nonwhite | 14 (10) | 12 (9) | 25 (11) | 28 (13) | |
| Hemoglobin, g/dL | | | | | .88 |
| Median | 9.3 | 9.5 | 9.3 | 9.2 | |
| Range | 4.8-13.1 | 6.0-15.0 | 4.3-41.6 | 3.0-14.7 | |
| Platelets, $x10^9$/L | | | | | .04 |
| Median | 61 | 69 | 60 | 51 | |
| Range | 15-510 | 4-850 | 7-673 | 4-989 | |
| WBC count, $x10^9$/L | | | | | <.001 |
| Median | 26.6 | 21.1 | 6.3 | 4.9 | |
| Range | 0.9-450.0 | 0.9-434.1 | 0.6-240.0 | 0.6-140.8 | |
| Percentage of blood blasts | | | | | .002 |
| Median | 41 | 48 | 33 | 24 | |
| Range | 0-97 | 0-99 | 0-98 | 0-99 | |
| Percentage of bone marrow blasts | | | | | <.001 |
| Median | 61 | 67 | 62 | 51 | |
| Range | 4-93 | 7-97 | 8-99 | 4-95 | |
| FAB category, no. (%) | | | | | <.001 |
| M0 | 1 (1) | 4 (4) | 11 (7) | 9 (6) | |
| M1 | 17 (16) | 23 (26) | 43 (27) | 26 (19) | |
| M2 | 37 (35) | 25 (28) | 58 (37) | 58 (41) | |
| M4 | 32 (30) | 21 (24) | 20 (13) | 20 (14) | |
| M5 | 17 (16) | 14 (16) | 20 (13) | 13 (9) | |
| M6 | 2 (2) | 2 (2) | 4 (3) | 13 (9) | |
| M7 | 0 (0) | 0 (0) | 1 (1) | 1 (1) | |
| Extramedullary involvement, no. (%) | 33 (24) | 27 (20) | 42 (20) | 42 (19) | .79 |

Abbreviations: WBC, white blood count; FAB, French-American-British classification.

* *P*-values for categorical variables are from Fisher's exact test, *P*-values for continuous variables are from the Kruskal-Wallis test.

**Table A4.** Multivariable Analyses for Outcome in Younger and Older Patients With Primary Acute Myeloid Leukemia

| Variable in Final Models | CR | | DFS | | OS | |
|---|---|---|---|---|---|---|
| | OR (95% CI) | *P* | HR (95% CI) | *P* | HR (95% CI) | *P* |
| Younger patients, n=818* | | | | | | |
| ELN† Intermediate-I *v* Favorable | 0.15 (0.08-0.29) | <.001 | 2.51 (1.92-3.27) | <.001 | 2.68 (2.08-3.46) | <.001 |
| Intermediate-II *v* Favorable | 0.18 (0.10-0.35) | <.001 | 1.89 (1.45-2.45) | <.001 | 1.73 (1.33-2.24) | <.001 |
| Adverse *v* Favorable | 0.05 (0.03-0.09) | <.001 | 4.35 (3.28-5.77) | <.001 | 5.06 (3.99-6.42) | <.001 |
| Age, each 10-year increase | 0.82 (0.69-0.96) | .02 | - | - | 1.16 (1.07-1.25) | <.001 |
| WBC count, each 50-unit increase | - | - | 1.17 (1.06-1.30) | .002 | 1.20 (1.09-1.31) | <.001 |
| Platelets, each 50-unit increase | - | - | 0.88 (0.81-0.95) | <.001 | - | - |
| Sex, male *v* female | - | - | - | - | 1.24 (1.03-1.48) | .02 |
| Extramedullary involvement, present *v* absent | - | - | - | - | 0.75 (0.61-0.94) | .01 |
| Older patients, n=732‡ | | | | | | |
| ELN† Intermediate-I *v* Favorable | 0.32 (0.18-0.56) | <.001 | 1.70 (1.26-2.93) | <.001 | 1.99 (1.54-2.56) | <.001 |
| Intermediate-II *v* Favorable | 0.31 (0.18-0.52) | <.001 | 1.62 (1.25-2.11) | <.001 | 1.93 (1.53-2.42) | <.001 |
| Adverse *v* Favorable | 0.11 (0.07-0.19) | <.001 | 2.60 (1.94-3.49) | <.001 | 3.69 (2.92-4.65) | <.001 |
| Age, each 10-year increase | - | - | - | - | 1.16 (1.02-1.32) | .02 |
| WBC count, each 50-unit increase | 0.73 (0.61-0.87) | <.001 | - | - | - | - |

NOTE: Odds ratios greater than (less than) 1.0 mean higher (lower) CR rate for the higher values of the continuous variables and the first category listed for the categorical variables. Hazard ratios greater than (less than) 1.0 indicate higher (lower) risk for relapse or death (DFS) or death (OS) for the higher values of the continuous variables and the first category listed for the categorical variables. Variables considered in the model were those significant at α=.20 from the univariable models.

Abbreviations: CR, complete remission; DFS, disease-free survival; OS, overall survival; OR, odds ratio; HR, hazard ratio; CI, confidence interval; ELN, European LeukemiaNet; WBC, white blood cell.

* Variables considered in the model for younger patients were as follows: for CR achievement, ELN Groups, age (in 10-year increments), sex (male *v* female), extramedullary involvement (present *v* absent); for DFS, ELN Groups, WBC count (in 50-unit increments), platelets (in 50-unit increments), extramedullary involvement (present *v* absent); for OS, ELN Groups, age (in 10-year increments), WBC count (in 50-unit increments), sex (male *v* female), extramedullary involvement (present *v* absent).

† The ELN classification was considered as a four-level categorical variable, for which the ELN Favorable Group was used as a reference group.

‡ Variables considered in the model for older patients were as follows: for CR achievement, ELN Groups, age (in 10-year increments), WBC count (in 50-unit increments), platelets (in 50-unit increments); for DFS, ELN Groups, platelets (in 50-unit increments), sex (male *v* female), extramedullary involvement (present *v* absent); for OS, ELN Groups, age (in 10-year increments), sex (male *v* female).

**Table A5**. Outcome of Younger (<60 Years) and Older (≥60 Years) Patients With Primary Acute Myeloid Leukemia According to Genetic Subsets Within the European LeukemiaNet Favorable Genetic Group

| Outcome | t(8;21) | inv(16) or t(16;16) | *NPM1*-mut/ *FLT3*-ITD$^-$ CN-AML | *CEBPA*-mut CN-AML* | *P* |
|---|---|---|---|---|---|
| Younger patients, n=339 | n=76 | n=111 | n=95 | n=57 | |
| Complete remission rate, no. (%) | 75 (99) | 109 (98) | 87 (92) | 53 (93) | .04[†] |
| Disease-free survival<br>Median, years<br>Disease-free at 3 years, % (95% CI) | 5.0<br>52 (40-63) | 4.0<br>52 (42-61) | 8.3<br>59 (48-68) | 5.0<br>56 (42-68) | .93[†] |
| Overall survival<br>Median, years<br>Alive at 3 years, % (95% CI) | 11.5<br>61 (49-70) | NR<br>73 (64-80) | 10.5<br>64 (54-73) | 9.1<br>61 (47-72) | .30[†] |
| Older patients, n=145 | n=19 | n=18 | n=79 | n=29 | |
| Complete remission rate, no. (%) | 18 (95) | 16 (89) | 66 (84) | 20 (69) | .13[†] |
| Disease-free survival<br>Median, years<br>Disease-free at 3 years, % (95% CI) | 1.0<br>33 (14-55) | 0.8<br>13 (2-33) | 1.1<br>26 (16-37) | 0.7<br>20 (6-39) | .21[†] |
| Overall survival<br>Median, years<br>Alive at 3 years, % (95% CI) | 1.5<br>47 (24-68) | 1.9<br>33 (14-55) | 1.7<br>34 (24-44) | 1.4<br>21 (8-37) | .02[‡] |

Abbreviations: mut, mutated; CN-AML, cytogenetically normal acute myeloid leukemia; CI, confidence interval; NR, not reached.

* Patients with a single *CEBPA* mutation and those with a double mutation (ie, two different mutations affecting both alleles of the gene) are included since the European LeukemiaNet guidelines do not distinguish between single and double *CEBPA* mutations.

[†] None of the adjusted pairwise comparisons, ie, t(8;21) *v* inv(16) or t(16;16), t(8;21) *v* *NPM1*-mut/*FLT3*-ITD$^-$ CN-AML, t(8;21) *v* *CEBPA*-mut CN-AML, inv(16) or t(16;16) *v* *NPM1*-mut/*FLT3*-ITD$^-$ CN-AML, inv(16) or t(16;16) *v* *CEBPA*-mut CN-AML and *NPM1*-mut/*FLT3*-ITD$^-$ CN-AML *v* *CEBPA*-mut CN-AML, yielded a statistically significant difference.

[‡] OS of patients with t(8;21) was significantly longer than OS of those with *CEBPA*-mut CN-AML (adjusted *P*=.03), and there was a trend for a longer OS of patients with inv(16) or t(16;16) compared with OS of *CEBPA*-mut CN-AML patients (adjusted *P*=.11). All other adjusted pairwise comparisons were not significant.

**Table A6**. Outcome of Younger (<60 Years) and Older (≥60 Years) Patients With Primary Acute Myeloid Leukemia According to Genetic Subsets Within the European LeukemiaNet Intermediate-I Genetic Group

| Outcome | *NPM1*-mut/ *FLT3*-ITD$^+$ | *NPM1*-wt/ *FLT3*-ITD$^-$ | *NPM1*-wt/ *FLT3*-ITD$^+$ | *P* |
|---|---|---|---|---|
| Younger patients, n=144 | n=79 | n=50 | n=15 | |
| Complete remission rate, no. (%) | 64 (81) | 36 (72) | 9 (60) | .15* |
| Disease-free survival<br>Median, years<br>Disease-free at 3 years, % (95% CI) | <br>0.6<br>28 (18-39) | <br>1.1<br>14 (5-27) | <br>0.9<br>22 (3-51) | .96* |
| Overall survival<br>Median, years<br>Alive at 3 years, % (95% CI) | <br>1.1<br>32 (22-42) | <br>1.4<br>28 (16-40) | <br>0.9<br>13 (2-35) | .23* |
| Older patients, n=136 | n=52 | n=68 | n=16 | |
| Complete remission rate, no. (%) | 39 (75) | 37 (54) | 7 (44) | .02† |
| Disease-free survival<br>Median, years<br>Disease-free at 3 years, % (95% CI) | <br>0.6<br>15 (6-28) | <br>0.9<br>5 (1-16) | <br>0.4<br>0 | NE‡ |
| Overall survival<br>Median, years<br>Alive at 3 years, % (95% CI) | <br>0.7<br>17 (9-29) | <br>1.2<br>9 (4-17) | <br>0.7<br>0 | .06* |

Abbreviations: mut, mutated; wt, wild-type; CI, confidence interval; NE, *P*-value could not be calculated because of small (<8 patients) sample sizes.

* None of the adjusted pairwise comparisons, ie, *NPM1*-mut/*FLT3*-ITD$^+$ *v* *NPM1*-wt/*FLT3*-ITD$^-$, *NPM1*-mut/*FLT3*-ITD$^+$ *v* *NPM1*-wt/*FLT3*-ITD$^+$ and *NPM1*-wt/*FLT3*-ITD$^-$ *v* *NPM1*-wt/*FLT3*-ITD$^+$, yielded a statistically significant difference.

† Patients with *NPM1*-mut/*FLT3*-ITD$^+$ had a higher CR rate, by trend, than CR rates of patients with *NPM1*-wt/*FLT3*-ITD$^-$ (adjusted *P*=.07) and those with *NPM1*-wt/*FLT3*-ITD$^+$ (adjusted *P*=.07). There was no significant difference in CR rates between *NPM1*-wt/*FLT3*-ITD$^+$ and *NPM1*-wt/*FLT3*-ITD$^-$ patients.

‡ There was no significant difference in disease-free survival between *NPM1*-mut/*FLT3*-ITD$^+$ and *NPM1*-wt/*FLT3*-ITD$^-$ patients. The remaining pairwise comparisons could not be made due to small sample sizes.

**Table A7.** Outcome of Younger (<60 years) and Older (≥60 years) Patients With Primary Acute Myeloid Leukemia According to Genetic Subsets Within the European LeukemiaNet Intermediate-II Genetic Group

| Outcome | t(9;11) | Other Abnormalities | *P* |
|---|---|---|---|
| Younger patients, n=156 | n=17 | n=139 | |
| Complete remission rate, no. (%) | 14 (82) | 109 (78) | 1.00 |
| Disease-free survival | | | .04 |
| Median, years | NR | 1.1 | |
| Disease-free at 3 years, % (95% CI) | 57 (28-78) | 31 (23-40) | |
| Overall survival | | | .20 |
| Median, years | NR | 2.0 | |
| Alive at 3 years, % (95% CI) | 53 (28-73) | 44 (36-52) | |
| Older patients, n=222 | n=12 | n=210 | |
| Complete remission rate, no. (%) | 11 (92) | 128 (61) | .03 |
| Disease-free survival | | | .03 |
| Median, years | 0.5 | 0.8 | |
| Disease-free at 3 years, % (95% CI) | 0 | 12 (7-18) | |
| Overall survival | | | .24 |
| Median, years | 0.8 | 1.0 | |
| Alive at 3 years, % (95% CI) | 8 (1-31) | 16 (11-21) | |

Abbreviations: CI, confidence interval; NR, not reached.

**Table A8.** Outcome of Younger (<60 Years) and Older (≥60 Years) Patients With Primary Acute Myeloid Leukemia According to Genetic Subsets Within the European LeukemiaNet Adverse Genetic Group

| Outcome | inv(3) or t(3;3) | t(6;9) | t(v;11) | –5 or del(5q)* | –7 | Complex† | *P*‡ |
|---|---|---|---|---|---|---|---|
| Younger patients, n=179 | n=15 | n=7 | n=26 | n=5 | n=9 | n=117 | |
| Complete remission rate, no. (%) | 3 (20) | 4 (57) | 21 (81) | 3 (60) | 3 (33) | 56 (48) | <.001§ |
| Disease-free survival | | | | | | | NE |
| Median, years | 0.7 | 0.7 | 0.7 | 1.6 | 0.8 | 0.5 | |
| Disease-free at 3 years, % (95% CI) | 0 | 0 | 19 (6-38) | 33 (1-77) | 0 | 7 (2-16) | |
| Overall survival | | | | | | | .09‖ |
| Median, years | 0.7 | 0.9 | 1.1 | 2.2 | 0.9 | 0.7 | |
| Alive at 3 years, % (95% CI) | 7 (0-26) | 14 (1-46) | 27 (12-44) | 40 (5-75) | 11 (1-39) | 9 (4-14) | |
| Older patients, n=229 | n=7 | n=1 | n=14 | n=8 | n=27 | n=172 | |
| Complete remission rate, no. (%) | 1 (14) | 1 (100) | 8 (57) | 0 (0) | 12 (44) | 67 (39) | .05¶ |
| Disease-free survival | | | | | | | .08** |
| Median, years | 0.5# | 0.2# | 0.5 | NA | 0.7 | 0.4 | |
| Disease-free at 3 years, % (95% CI) | 0 | 0 | 25 (4-56) | NA | 0 | 5 (1-11) | |
| Overall survival | | | | | | | .10** |
| Median, years | 0.7 | 0.9# | 0.8 | 0.5 | 0.7 | 0.4 | |
| Alive at 3 years, % (95% CI) | 0 | 0 | 14 (2-37) | 0 | 0 | 3 (1-7) | |

Abbreviations: CI, confidence interval; NA – not available; NE – *P*-value could not be calculated because of small (less than 8 patients) sample sizes.

* No patient in our study had –5. Likewise, no patient had abnormality of 17p, which is why this Subset is not included in the Table.

† Complex karyotype is defined as three or more chromosome abnormalities in the absence of one of the World Health Organization designated recurring translocations or inversions, that is, t(8;21), inv(16) or t(16;16), t(15;17), t(9;11), t(v;11)(v;q23), t(6;9), inv(3) or t(3;3).

‡ Overall *P*-values are unadjusted and include only groups with sample sizes of 8 or more patients.

§ CR rate of patients with t(v;11) was significantly higher than CR rates of patients with inv(3) or t(3;3) (adjusted *P*=.001) and those with a complex karyotype (adjusted *P*=.01), and there were trends for higher CR rates of patients with t(v;11) compared with a CR rate of patients with –7 (adjusted *P*=.06), and of patients with a complex karyotype compared with CR rate of patients with inv(3) or t(3;3) (adjusted *P*=.16). All other adjusted pairwise comparisons were not significant.

‖ Patients with a complex karyotype had shorter OS, by trend, than OS of patients with –7 (adjusted *P*=.10). All other adjusted pairwise comparisons were not significant.

¶ CR rate of patients with del(5q) was lower, by trend, than CR rates of patients with t(v;11) (adjusted *P*=.11), patients with –7 (adjusted *P*=.13) and those with a complex karyotype (*P*=.13). All other adjusted pairwise comparisons were not significant.

# This is survival of one patient.

** None of the adjusted pairwise comparisons yielded a statistically significant difference.

## SUPPLEMENTAL FIGURES

**Fig A1.** Comparison of outcomes of younger and older patients with primary acute myeloid leukemia classified into selected European LeukemiaNet Genetic Groups. (A) Disease-free and (B) overall survival of younger patients in the Intermediate-I Group are similar to those of older patients in the Favorable Group, as are (C) disease-free and (D) overall survival of younger patients in the Adverse Group and older patients in the Intermediate-I and Intermediate-II Groups.

**Fig A2.** Outcome of patients with primary acute myeloid leukemia classified according to the Genetic Subsets within the European LeukemiaNet Favorable Genetic Group. (A) Disease-free survival and (B) overall survival of patients aged <60 years. (C) Disease-free survival and (D) overall survival of patients aged ≥60 years.

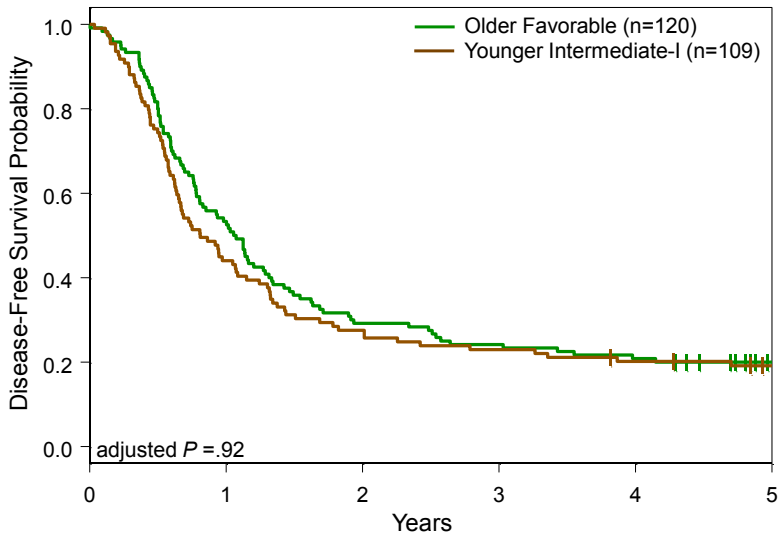
**Fig A3**. Outcome of patients with primary acute myeloid leukemia classified according to the Genetic Subsets within the European LeukemiaNet Intermediate-I Genetic Group. (A) Disease-free survival and (B) overall survival of patients aged <60 years. (C) Disease-free survival and (D) overall survival of patients aged ≥60 years. NE denotes a *P*-value that could not be calculated because of small sample sizes.

**Fig A4.** Outcome of patients with primary acute myeloid leukemia classified according to the Genetic Subsets within the European LeukemiaNet Intermediate-II Genetic Group. (A) Disease-free survival and (B) overall survival of patients aged <60 years. (C) Disease-free survival and (D) overall survival of patients aged ≥60 years.

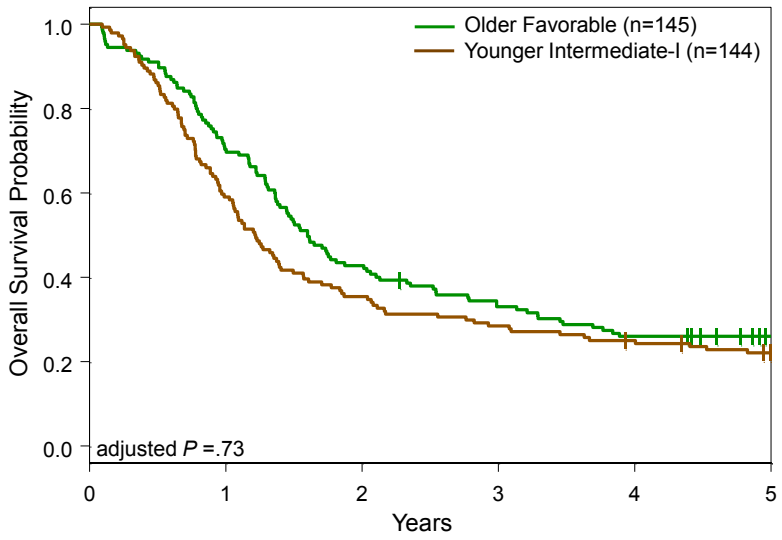
**Fig A5.** Outcome of patients with primary acute myeloid leukemia classified according to the Genetic Subsets within the European LeukemiaNet Adverse Genetic Group. (A) Disease-free survival and (B) overall survival of patients aged <60 years. (C) Disease-free survival and (D) overall survival of patients aged ≥60 years. NE denotes a *P*-value that could not be calculated because of small (less than 8 patients) sample sizes.

**Fig A1.**

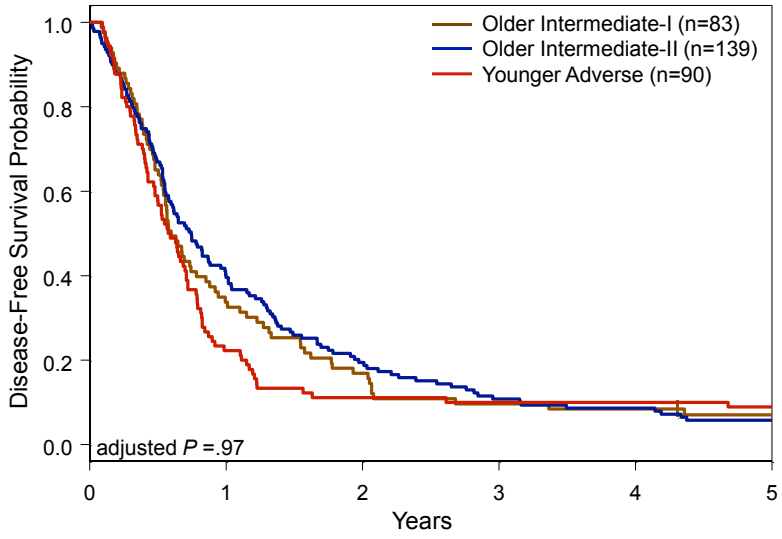
**A**


Older Favorable (n=120)
Younger Intermediate-I (n=109)
Disease-Free Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
adjusted P =.92
0
1
2
3
4
5
Years

**B**


Older Favorable (n=145)
Younger Intermediate-I (n=144)
Overall Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
adjusted P =.73
0
1
2
3
4
5
Years

**C**


Older Intermediate-I (n=83)
Older Intermediate-II (n=139)
Younger Adverse (n=90)
Disease-Free Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
adjusted P =.97
0
1
2
3
4
5
Years

**D**

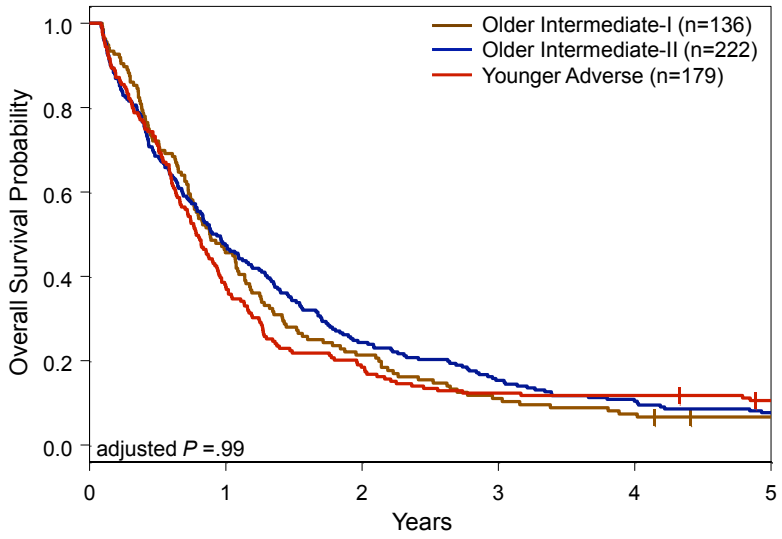
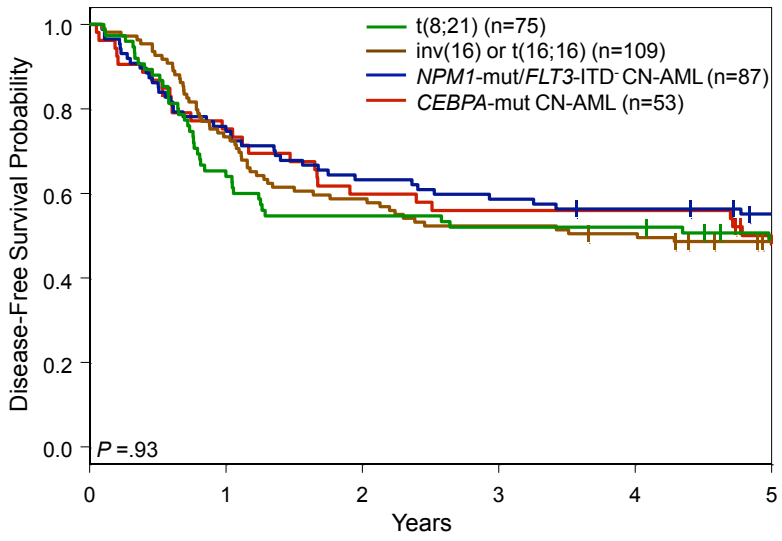
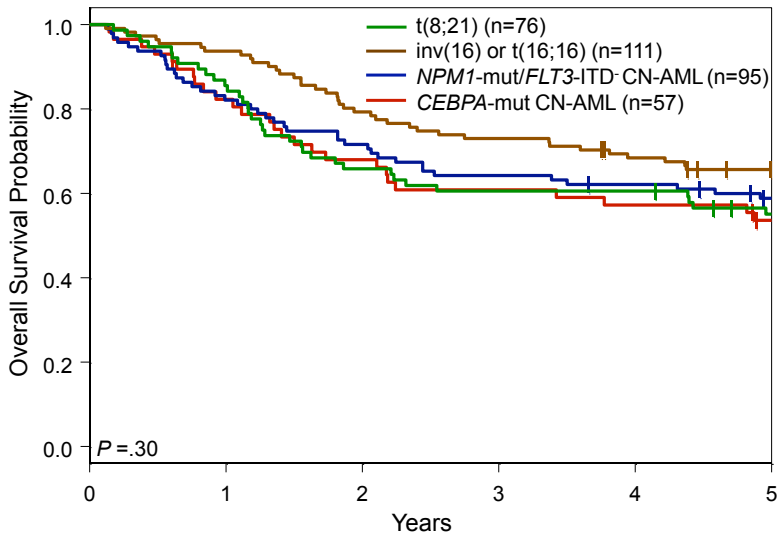

Older Intermediate-I (n=136)
Older Intermediate-II (n=222)
Younger Adverse (n=179)
Overall Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
adjusted P =.99
0
1
2
3
4
5
Years

**Fig A2.**

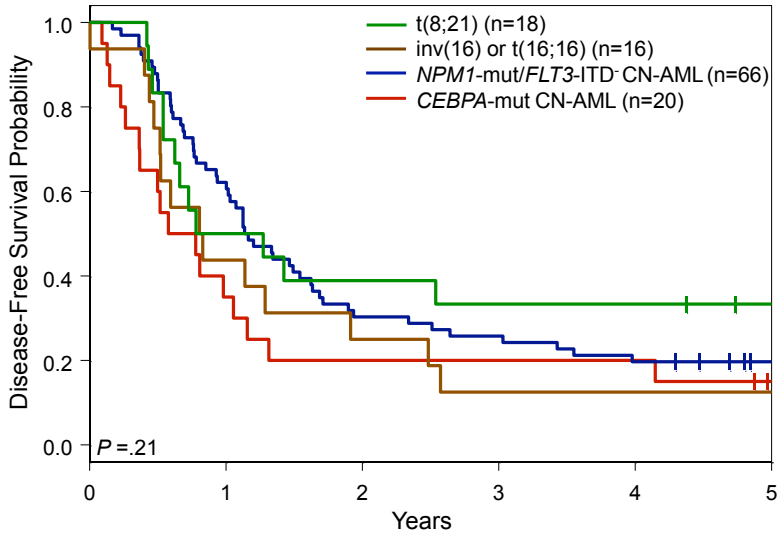
**A**


t(8;21) (n=75)
inv(16) or t(16;16) (n=109)
*NPM1*-mut/*FLT3*-ITD- CN-AML (n=87)
*CEBPA*-mut CN-AML (n=53)
Disease-Free Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
*P* =.93
0
1
2
3
4
5
Years

**B**


t(8;21) (n=76)
inv(16) or t(16;16) (n=111)
*NPM1*-mut/*FLT3*-ITD- CN-AML (n=95)
*CEBPA*-mut CN-AML (n=57)
Overall Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
*P* =.30
0
1
2
3
4
5
Years

**C**


t(8;21) (n=18)
inv(16) or t(16;16) (n=16)
*NPM1*-mut/*FLT3*-ITD- CN-AML (n=66)
*CEBPA*-mut CN-AML (n=20)
Disease-Free Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
*P* =.21
0
1
2
3
4
5
Years

**D**

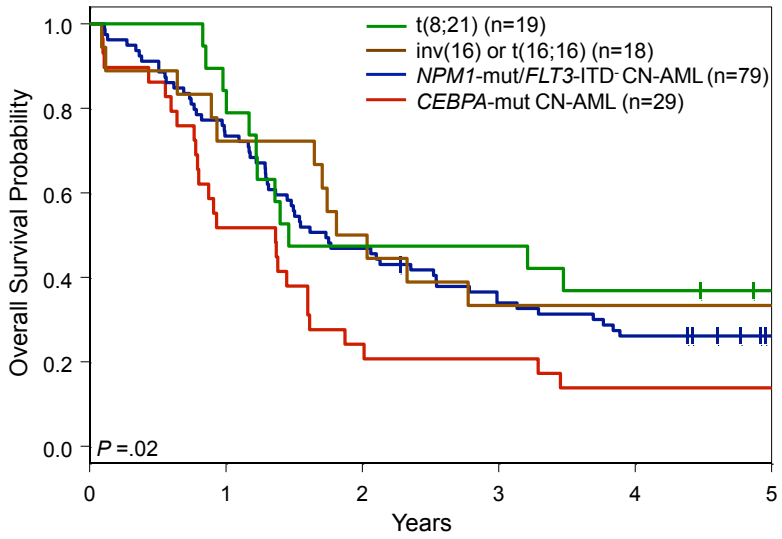
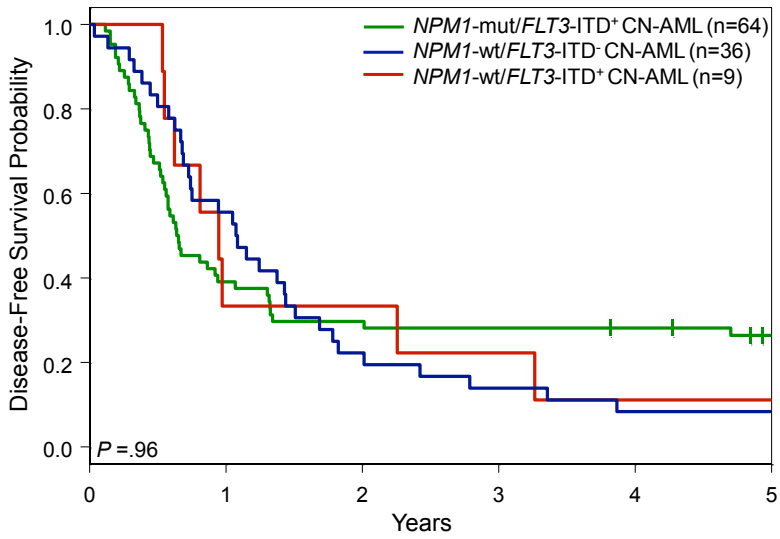
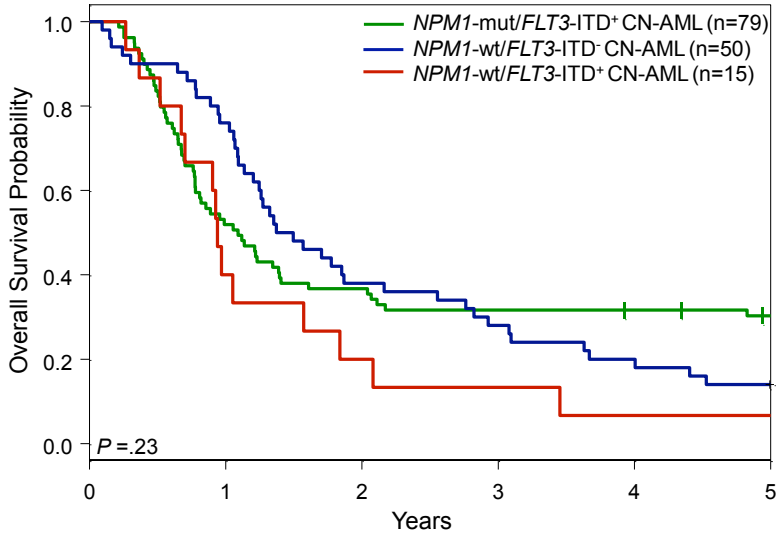

t(8;21) (n=19)
inv(16) or t(16;16) (n=18)
*NPM1*-mut/*FLT3*-ITD- CN-AML (n=79)
*CEBPA*-mut CN-AML (n=29)
Overall Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
*P* =.02
0
1
2
3
4
5
Years

**Fig A3.**

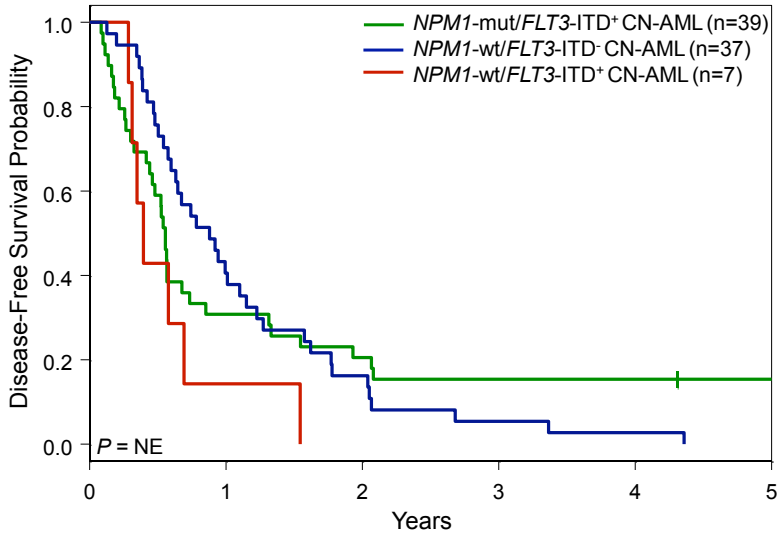
**A**


NPM1-mut/FLT3-ITD+ CN-AML (n=64)
NPM1-wt/FLT3-ITD- CN-AML (n=36)
NPM1-wt/FLT3-ITD+ CN-AML (n=9)
Disease-Free Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
P =.96
0
1
2
3
4
5
Years

**B**


NPM1-mut/FLT3-ITD+ CN-AML (n=79)
NPM1-wt/FLT3-ITD- CN-AML (n=50)
NPM1-wt/FLT3-ITD+ CN-AML (n=15)
Overall Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
P =.23
0
1
2
3
4
5
Years

**C**


*NPM1*-mut/*FLT3*-ITD+ CN-AML (n=39)
*NPM1*-wt/*FLT3*-ITD- CN-AML (n=37)
*NPM1*-wt/*FLT3*-ITD+ CN-AML (n=7)
Disease-Free Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
*P* = NE
0
1
2
3
4
5
Years

**D**

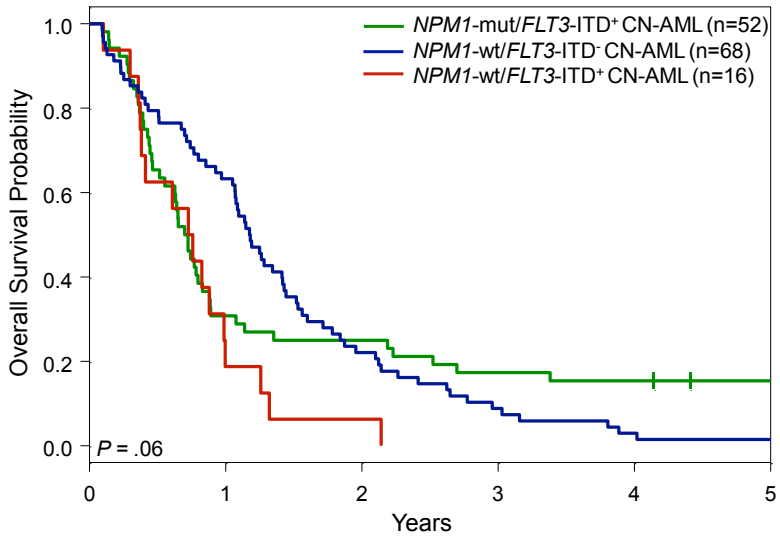
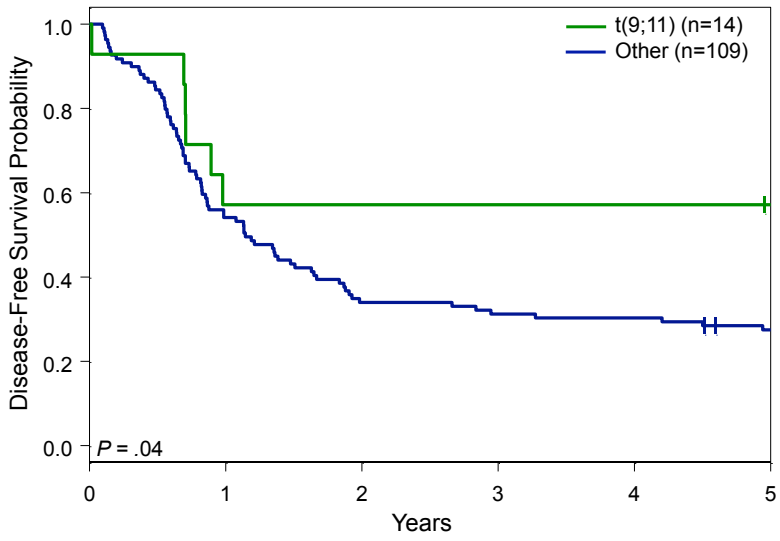
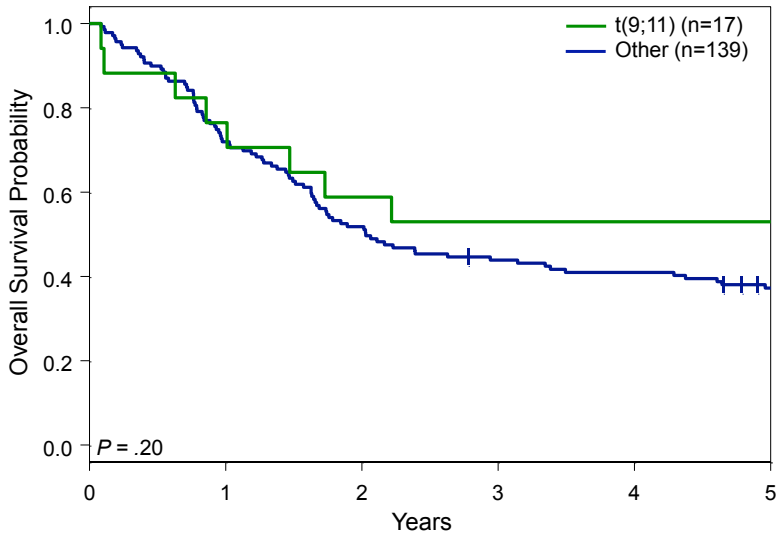

*NPM1*-mut/*FLT3*-ITD+ CN-AML (n=52)
*NPM1*-wt/*FLT3*-ITD- CN-AML (n=68)
*NPM1*-wt/*FLT3*-ITD+ CN-AML (n=16)
Overall Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
*P* = .06
0
1
2
3
4
5
Years

**Fig A4.**

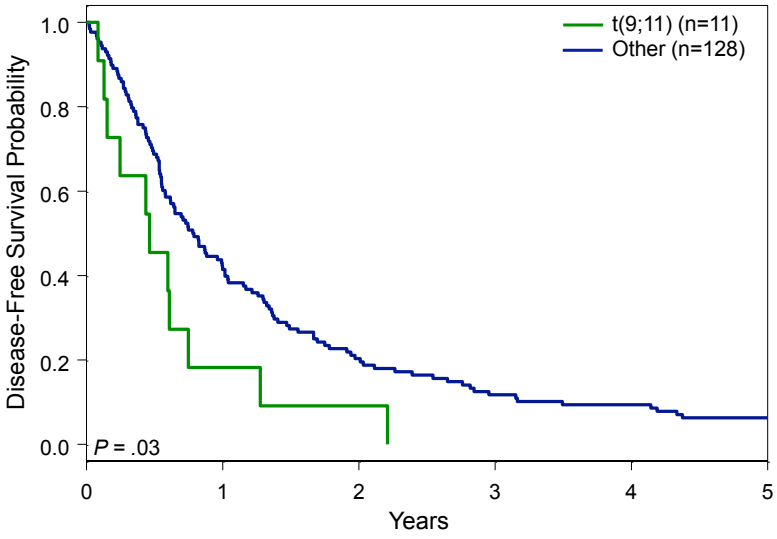
**A**


t(9;11) (n=14)
Other (n=109)
Disease-Free Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
P = .04
0
1
2
3
4
5
Years

**B**


t(9;11) (n=17)
Other (n=139)
Overall Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
P = .20
0
1
2
3
4
5
Years

**C**


t(9;11) (n=11)
Other (n=128)
Disease-Free Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
P = .03
0
1
2
3
4
5
Years

**D**

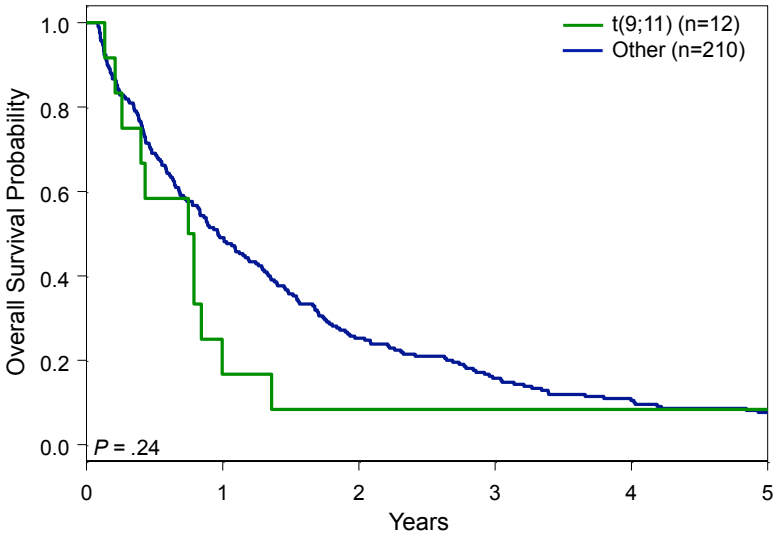
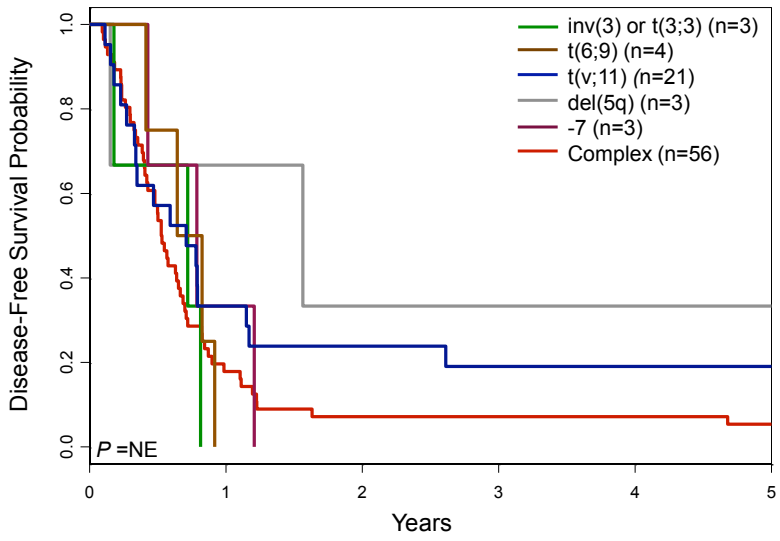
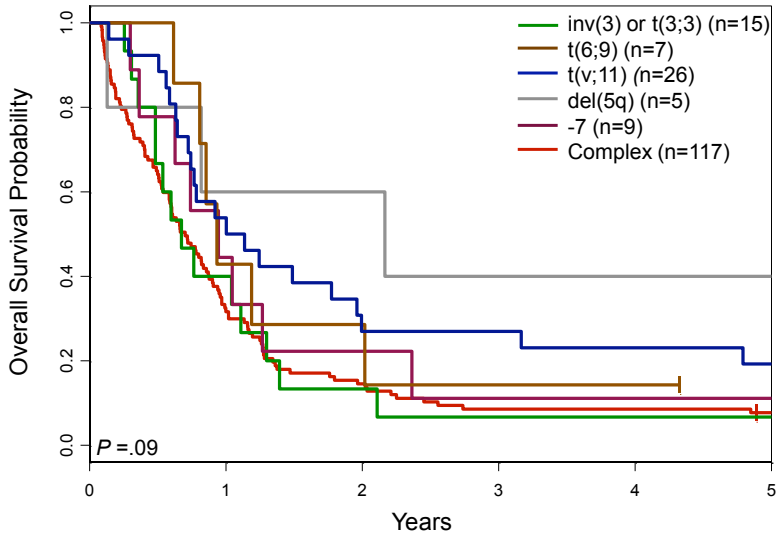

t(9;11) (n=12)
Other (n=210)
Overall Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
P = .24
0
1
2
3
4
5
Years

**Fig A5.**

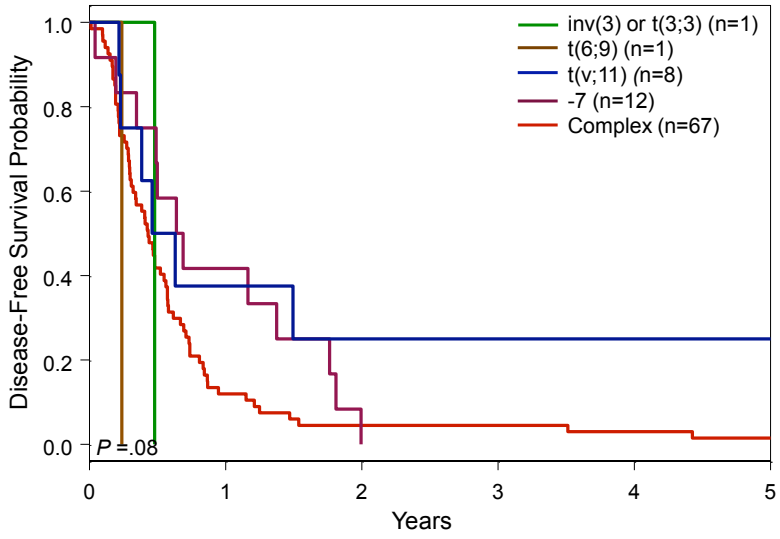
**A**


Disease-Free Survival Probability
0.0
0.2
0.4
0.6
0.8
1.0
0
1
2
3
4
5
Years
P =NE
inv(3) or t(3;3) (n=3)
t(6;9) (n=4)
t(v;11) (n=21)
del(5q) (n=3)
-7 (n=3)
Complex (n=56)

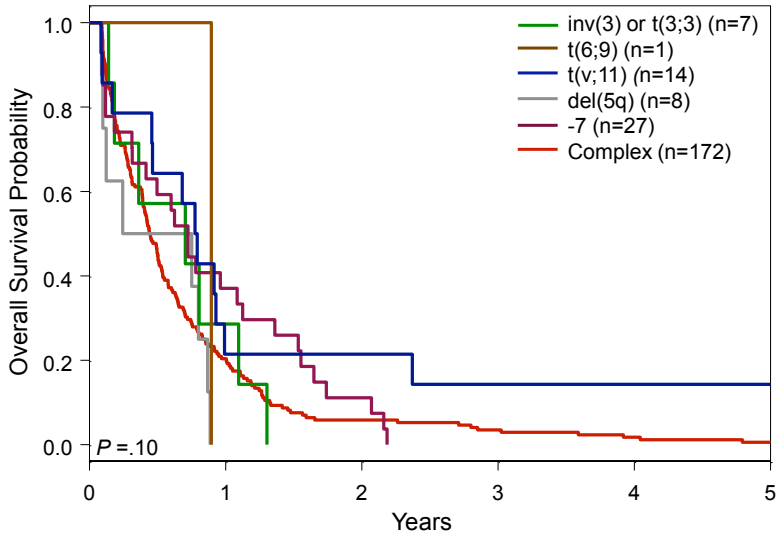
**B**


Overall Survival Probability
0.0
0.2
0.4
0.6
0.8
1.0
0
1
2
3
4
5
Years
P =.09
inv(3) or t(3;3) (n=15)
t(6;9) (n=7)
t(v;11) (n=26)
del(5q) (n=5)
-7 (n=9)
Complex (n=117)

**C**


Disease-Free Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
P =.08
0
1
2
3
4
5
Years
inv(3) or t(3;3) (n=1)
t(6;9) (n=1)
t(v;11) (n=8)
-7 (n=12)
Complex (n=67)

**D**


Overall Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
P =.10
0
1
2
3
4
5
Years
inv(3) or t(3;3) (n=7)
t(6;9) (n=1)
t(v;11) (n=14)
del(5q) (n=8)
-7 (n=27)
Complex (n=172)