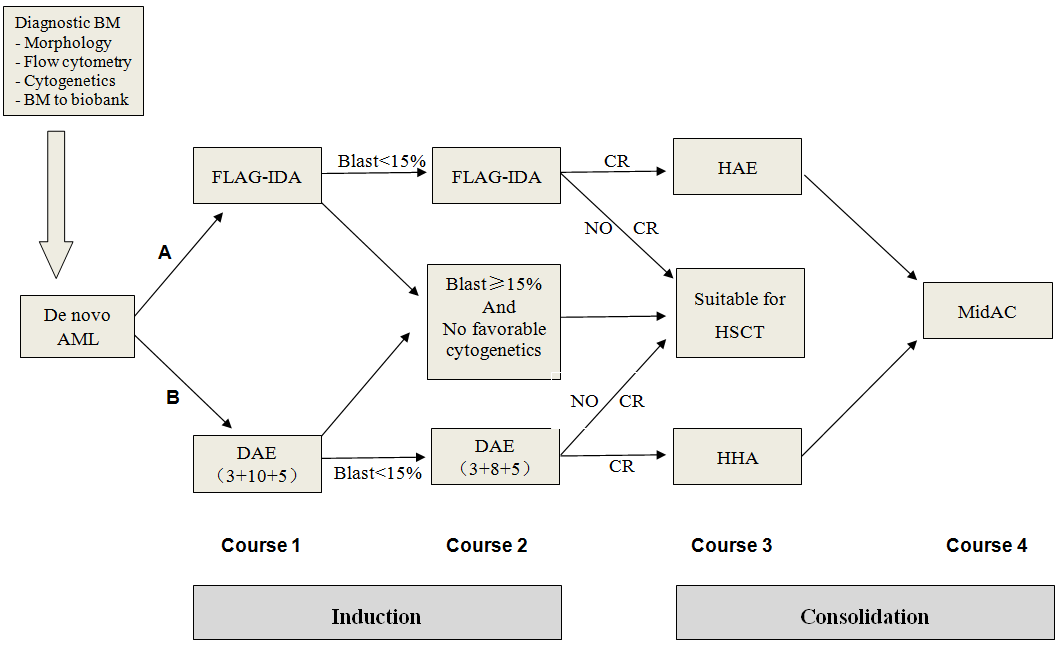
**Table S1. Prognostic risk systems in C-HUANAN-AML15 protocol**

|  |  |
| --- | --- |
| Risk stratification | Genetic abnormality and induction chemotherapy response |
| Low risk criteria | Include one of the f0llowing genetic abnormality and CR after induction 1: t(8;21)(q22;q22)；AML/ETO（RUNX1- RUNX1T1）;  inv(16)(p13q22)/t(16;16)(p13;q22)；CBFB-MYH11；  normal cytogenetics: NPM1 or isolated biallelic (double) CEBPA mutation in the absence of FLT3-ITD |
| Intermediate risk criteria | Exclude low risk or high risk genetic abnormality and blast in bone＜15% after induction1 and CR after induction2 |
| High risk criteria | Include one of the f0llowing genetic abnormal blast in bone≥15% after induction1 or no CR after induction2:  Mutated FLT3-ITD;  Complex karyotype;  -5 or del(5q);  abn(3q);  abn(17p);  -7 or del(7q) |

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**Figure S1 C-HUANAN-AML15 protocol workflow. FLAG-IDA: Fludarabine 30 mg/m2/d d2-6, cytarabine 2g/ m2/d d2-6, Idarubicin 8 mg/m2/d d4-6, Granulocyte Colony Stimulating Factor (G-CSF) 5μg/kg/d d1-7. DAE (3+10+5): Daunorubicin 50 mg/m2/d d1,3,5; Cytarabine 100mg/m2 q12h d1-10, Etoposide 100mg/m2/d d1-5. DAE (3+8+5): Daunorubicin 50 mg/m2/d d1,3,5; Cytarabine 100mg/m2 q12h d1-8, Etoposide 100mg/m2/d d1-5. HAE: Homoharringtonine 3mg/m2/d d1-5, Cytarabine 100mg/m2 q12h d1-7, Etoposide 100mg/m2/d d1-5. HHA: Homoharringtonine 3mg/m2/d d1-7, Cytarabine 2g/m2 q12h d1-3. MidAc: Mitoxantrone 10mg/m2/d d1-5, Cytarabine 1g/m2 q12h d1-3.**

**Table S2. Clinical and Genetic Characteristics According to EVI1 Status in patients with MLL rearrangement.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Characteristic | MLL patients (n=70) | EVI1high group (n=15) | EVI1low group (n=55) | *P* |
| Age, months |  |  |  | 0.584 |
| Median (range) | 44.5(8-168) | 60(12-163) | 42(8-168) |  |
| Sex, n% |  |  |  | 1.000 |
| Male | 41(58.6) | 9(60.0) | 32(58.2) |  |
| Female | 29(41.4) | 6(40.0) | 23(41.8) |  |
| WBC, ×109/L |  |  |  | 1.000 |
| <50 | 47(67.1) | 10(66.7) | 37(67.3) |  |
| ≥50 | 23(32.9) | 5(33.3) | 18(32.7) |  |
| FAB subtype, n% |  |  |  | 1.000 |
| M7 | 4(5.7) | 1(6.7) | 3(5.5) |  |
| Other types | 66(94.3) | 14(93.3) | 52(94.5) |  |
| \*Cytogenetic characteristics, n(%) |  |  |  |  |
| -7 or del(7q) | 1(1.4) | 1(6.7) | 0(0) | 0.214 |
| Complex karyotype | 2(2.9) | 1(6.7) | 1(1.8) | 1.000 |
| †Cytogenetic risk |  |  |  | 0.020 |
| Intermediate | 38(54.3) | 4(26.7) | 34(61.8) |  |
| Unfavorable | 32(45.6) | 11(73.3) | 21(38.2) |  |
| Molecular abnormalities |  |  |  |  |
| FLT3-ITD | 5(7.1) | 2(13.3) | 5(5.5) | 0.577 |
| ASXL1 | 8(11.4) | 0(0) | 8(14.5) | 0.187 |
| CEBPA- mutation | 1(1.4) | 0(0) | 1(1.8) | 1.000 |
| CR after induction 2nd |  |  |  | 0.348 |
| Yes | 60(85.7) | 11(73.3) | 49(89.1) |  |
| No | 5(7.1) | 2(13.3) | 3(5.5) |  |
| Missing | 5(7.1) | 2(13.3) | 3(5.5) |  |
| Blast>15% in BM after induction 1st |  |  |  | 0.494 |
| Yes | 5(7.1) | 2(13.3) | 3(5.5) |  |
| No | 64(91.4) | 13(86.7) | 51(92.7) |  |
| Missing | 1(1.4) | 0(0) | 1(1.8) |  |

**\*** **Patients may be counted more than once owing to the coexistence of more than one cytogenetic abnormality in the leukemic clone.**

**†Favorable risk: t(15;17), t(8;21), inv(16)/t(16;16); unfavorable risk: inv(3) or t(3;3), t(6;9), t(v;11q23) other than t(9;11), -5 or del(5q), -7 or del(7q), abn(17p), complex karyotype (three or more abnormalities in the absence of a WHO designated recurring chromosome abnormality); intermediate risk: all chromosome abnormalities not classified as favorable or unfavorable. #Only 383 patients were included in this part, for 38 cases giving up treatment or loss to follow-up.**

**Table S3. Univariate and multivariate analysis of patients with MLL-AF9 rearrangement.**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Cases (n=29) | EFS | | | | OS | | | | |
| **Univariate Analysis** | **HR** | **95% CI** | ***P* value** | | **HR** | **95% CI** | | ***P* value** | |
| Age (+1 year) | 0.988 | 0.960-1.016 | | 0.396 | 0.993 | | 0.965-1.020 | | 0.593 | |
| Gender (Male) | 3.386 | 0.376-30.456 | | 0.277 | 2.516 | | 0.260-24.359 | | 0.426 | |
| WBC (≥50X109/L) | 4.080 | 0.678-24.572 | | 0.125 | 5.464 | | 0.768-38.886 | | 0.090 | |
| FAB (M7) | 2.300 | 0.254-20.813 | | 0.458 | 2.989 | | 0.303-29.520 | | 0.349 | |
| Risk Category1\* | 2.526 | 0.279-22.835 | | 0.409 | 2.883 | | 0.299-27.770 | | 0.360 | |
| Risk Category2@ | 4.635 | 0.774-27.761 | | 0.093 | 8.484 | | 0.882-81.632 | | 0.064 | |
| EVI1high | 7.112 | 1.182-42.794 | | 0.032 | 13.349 | | 1.384-128.742 | | 0.025 | |
| ASXL1 mutation | 0.034 | 0.000-372.842 | | 0.477 | 0.035 | | 0.000-1310.839 | | 0.533 | |
| Induction protocol (DAE) | 14.337 | 1.598-128.614 | | 0.017 | 10.209 | | 1.061-98.231 | | 0.044 | |
| No CR after 2nd course | 25.456 | 1.590-407.465 | | 0.022 | 25.456 | | 1.590-407.465 | | 0.022 | |
| Blast>15% in BM after 1st course | 4.061 | 0.449-36.725 | | 0.212 | 5.179 | | 0.533-50.307 | | 0.156 | |
| **Multivariate Analysis** | **HR** | **95% CI** | ***P* value** | | **HR** | **95% CI** | | ***P* value** | |
| EVI1high | 10.091 | 0.858-118.713 | 0.066 | | 13.056 | 0.901-189.160 | | 0.060 | |
| Induction protocol (DAE) | 18.317 | 1.370-244.949 | 0.028 | | 9.792 | 0.676-141.870 | | 0.094 | |
| No CR after 2nd course | 2.092 | 0.115-38.204 | 0.618 | | 2.188 | 0.117-40.812 | | 0.600 | |

\*Risk category based on treatment regimens. Refer to Supplementary TableS1.

@ Risk category based on cytogenetic stratification of ELN 2017.

**Table S4. The similarities and differences regarding *EVI1*high in pediatric *vs* adult AML**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Pediatric AML | | Adult AML |
| Incidence (%) | | 9~28(1-3) | 7.8~15.4%(4, 5) |
| Associated with FAB type | | M7(1), M4/5/7(2), M6/7(3) | M5(6) |
| Associated with 3q26 abnormalities | | no 3q26 abnormalities were identified in *EVI1high* pediatric AML(1-3), 2.6% (1/38) 3q26 abnormality was identified in our study. | *EVI1high* was found in 65% 3q AML and 45% 3q26 AML(5); 3q26 was significant higher in *EVIhigh* AML than *EVIlow* AML (15.4% vs 0.2%, *P*<0.001)(4). |
| Associated with *MLL-r* | | *EVI1high* was detected in 27.7%~36% AML patients with *MLL-r* and 37.9% in patients with *MLL-AF9* (3, 7); and *MLL-r* occurred in 40% of *EVI1high* patients as opposed to 12% of the *EVI1low* patients (*P*<0.001)(1). | *EVI1high* was found in 45.8% of all patients with *MLL-r*, with *MLL-AF6* showing the highest frequency (83.9%), followed by *MLL-AF9* at 40.0%(8); and *MLL-r* occurred in 13.2% of *EVI1high* patients as opposed to 1.3% of the *EVI1low* patients (*P*<0.001)(4). |
| Associated with other cytogenetic Abnormalities | | *EVI1high* was virtually absent in favourable-risk AML, including core-binding factor AML, t(15;17), double mutations in the myeloid transcription factor gene *CEBPA* or mutations in nucleophosmin (*NPM1*) without concurrent mutation in the haematopoietic receptor *FLT3*, but significantly associated with monosomy 7(3-5). | |
| Prognosis value | | *EVI1high* patients had significantly lower EFS and OS. However, in multivariate analysis including other established prognostic markers, *EVI1* expression did not retain independent prognostic significance(1, 3). | *EVI1high* has been shown to act as an independent adverse prognostic marker for complete remission (CR), overall- (OS), relapse free- (RFS) and event-free (EFS) survival in AML, i.e., irrespective of the presence of 3q26 rearrangements(4, 5). Moreover, *EVI1high* defines poor prognostic subsets among AML with *MLL-r* and AML with *MLL-AF9*(8). |
| Allogeneic hematopoietic stem cell transplantation (all-HSCT) | | There was no aveilable study in literature about whether HSCT could improve suvival outcome of pediatric AML patients with *EVI1high*. In our study, patients with *EVI1high* who underwent allo-HSCT after CR1 had higher OS and EFS than those who only received chemotherapy, but the difference was not statistically significant. (EFS: 68.4% vs. 50.8%, *p* = 0.26; OS: 65.9% vs. 54.8%, *p* = 0.45) | Patients with *EVI1high* AML, especially in *MLL-r* subtype seem to benefit from allo-HSCT in first CR(4, 8). |

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