**SUPPLEMENTAL MATERIAL**

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# Table S1: Intrathecal therapy

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  AGE DRUG | 0 to 1 year | 1 to 2 years | 2 to 3 years | 3 to 10 years | > 10 years |
| METHYLPREDNISOLONE | 20 mg | 20 mg | 20 mg | 20 mg | 20 mg |
| METHOTREXATE | 6 mg | 8 mg | 10 mg | 12 mg | 15 mg |
| CYTARABINE | 12 mg | 15 mg | 20 mg | 25 mg | 30 mg |

# Table S2: Risk group defined according to the amendment

|  |  |  |
| --- | --- | --- |
|  Standard risk | Intermediate risk | High risk |
|  - t(8;21)(q22;q22) or inv16 (p13;q22) or t(16;16)AND- MRD after course 1 (>3 log reduction) | None criteria from standard or high risk groups | - monosomy 7- abn5q- t(6;9)(p23;q34)- t(10;11)(p11-14;q23)- t(6;11)(q27;q23)- inv(3)(q21q26) or t(3;3)(q21;q26)- Complex karyotype  (≥3 abnormalities) |
| * Normal karyotype

AND* NPM1 mutation

AND* No FLT3-ITD
 |
| * Normal karyotype

AND* CEBPA double mutation

AND* No FLT3-ITD
 | CR no reached after course 2, but in CR before SCT |
| t(1;11) (q21;q23) |
| t(9;11) (p21-22;q23) without any other cytogenetics abnormality ANDWBC < 50 G/l at diagnosisANDAbsence of CNS involvement |  FLT3-ITD with allelic ratio > 0.4 |

# Table S3: Comparison of baseline characteristics between randomized patients and not randomized patients

| Characteristic | RandomizedN=154 | Not randomizedN=90 | p-value |
| --- | --- | --- | --- |
|  |  |  |  |
| Age (year) | 7.3 ± 5.5 | 8.6 ± 5.7 | 0.0772 |
| Female sex | 67 (43.5) | 40(44.4) | 0.8867 |
| FAB subtype |  |  | 0.3269 |
| M0 | 6 (3.9) | 2 (2.2) |  |
| M1 | 22 (14.3) | 18 (20.0) |  |
| M2 | 41 (26.6) | 18 (20.0) |  |
| M4 | 29 (18.8) | 20 (22.2) |  |
| M5 | 43 (27.9) | 20 (22.2) |  |
| M6 | 2 (1.3) | 1 (1.1) |  |
| M7 | 7 (4.5) | 8 (8.9) |  |
| Isolated myeloid sarcoma | 0 (0.0) | 2 (2.2) |  |
| Unclassable or other | 4 (2.6) | 1 (1.1) |  |
| WBC (G/L) |  |  |  |
| Median | 14.2 [5.8 ; 64.2] | 20.3 [9.7 ; 62.2] | 0.0738 |
| > 30 G/L | 56 (36.4) | 36 (40.0) | 0.5717 |
| CNS involvement | 25 (16.2) | 16 (17.8) | 0.7556 |
| Karyotype | 153/154 | 88/90 | 0.4535 |
| Standard risk | 55 (35.9) | 28 (31.8) |  |
| Intermediate risk | 71 (46.4) | 48 (54.5) |  |
| High risk | 27 (17.7) | 12 (13.6) |  |

*Data are n (%) or mean ± standard deviation or median [interquartile range]*

# Figure S1: IL2+ patients’ detailed flow chart



# Table S4. Randomized trials of IL-2 monotherapy versus no treatment (standard-of-care) as remission maintenance in AML patients in CR1

This table is inspired and modified from Buyse et al(1). Results of ELAM02 phase III randomized trial are integrated.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Trial (NCT)\* | n | Median follow-up (months) | Age(years) | IL-2 regimen | Planned monthly dose (MIU/m2) x no. of months | Results, IL-2 vs controls† | *P*, IL-2vs controls |
|  |  |  |  |  |  |  |  |
| Blaise et al (2) | 78 | 80 | <50 | Cycle 1: 12 MIU/m2 QD X 5 days followed by 4 cycles of 2 days each | 120 X 2 | 7-yr LFS: 30% vs 36%7-yr OS: 38% vs 47% | LFS *P* = .54OS *P* = .65 |
|  |  |  |  |  |  |  |  |
| ALFA 980 (3) | 161 | 40 | 50-70 | 5 MIU/m2 QD X 5 days/month | 25 X 12 | 4-yr EFS‡: 28% vs 32%4-yr OS: 41% vs 47% | EFS *P* = .88OS *P* = .14 |
|  |  |  |  |  |  |  |  |
| CALGB 9720(4) (NCT00003190) | 163 | 100 | ≥60 | 0.9 MIU/m2 QD X 10-14 days; followed by pulses of 12 MIU/m2 QD X 3 days between each 14-day cycle | 82 X 3 | No difference in median LFS = 6.1 monthsNo difference in medianOS = 14.7 months | LFS *P* = .47OS *P* = .61 |
|  |  |  |  |  |  |  |  |
| CALGB 19808(5)(NCT00006363) | 214 | 69 | < 60 | 1 MIU/m2 QD X 10-14 days; followed by pulses of 12-15 MIU/m2 QD X 3 days between each 14-day cycle | 91 X 3 | 3-yr LFS: 56% vs 45%3-yr OS: 68% vs 61% | LFS *P* = .11OS *P* = .09 |
|  |  |  |  |  |  |  |  |
| CCG-2961(6)(NCT00002798) | 289 | 54 | ≤21 | 9 MIU/m2 QD X 4 days then 1.6 MIU/m2 QD days 8-17  | 52 X 0.6 | 5-yr LFS: 51% vs 58%5-yr OS: 70% vs 73% | LFS *P* = .49 OS *P* = .73 |
|  |  |  |  |  |  |  |  |
| EORTC-GIMEMA 6991(7)(NCT00004128) | 550 | 43 | < 61 | 2.3-4.6 MIU/m2 QD X 5 days/month | 12-24 X 12 | 3-yr LFS: 44% vs 42%3-yr OS: 54% vs 56% | LFS *P* = .57OS *P* = .94 |
|  |  |  |  |  |  |  |  |
| ELAM02 | 154 | 55 | ≤18 | 2.5 MIU/m² QD X 1 day; followed by 5 MIU/m² QD X 4 days/month | 22.5 X 12 | 4-yr DFS: 66% vs 62%4-yr OS: 85% vs 88% | DFS *P* =0.74OS *P* =0.49 |

AML indicates acute myeloid leukemia; LFS, leukemia-free survival; MIU, millions of international units; OS, overall survival; and QD, once daily.

\*ClinicalTrials.gov registry number if available.

†IL-2 versus standard-of-care (no treatment).

‡EFS calculated as the date from randomization to the date of CR achievement failure, first relapse, or death.

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