**SUPPLEMENTARY TABLES**

Supplementary Table 1. Clinical and biological characteristics of individual patients included in the study.

| ID     | Sex | Age | FAB  | CD34 | Karyotype            | FLT3 | NPM1 |
|--------|-----|-----|------|------|----------------------|------|------|
|        |     |     |      |      | High-risk patients, i.e. adverse cytogenetic abnormalities |      |      |
| A1-P105| F   | 64  | M1   | +    | Complex\(^2\)        | WT   | WT   |
| A2-P112| F   | 51  | M0   | +    | Complex              | WT   | WT   |
| A3-P114| M   | 72  | M1   | +    | Complex              | WT   | -    |
| A4-P117| F   | 64  | M1   | +    | Complex              | ITD  | WT   |
| A5-P122| M   | 84  | M1   | +    | Complex              | WT   | WT   |
| A6-P130| M   | 78  | M0   | -    | Complex              | WT   | WT   |
| A7-P133| M   | 74  | M4   | -    | Complex              | WT   | -    |
| A8-P134| M   | 80  | M1   | +    | Complex              | -    | -    |
| A9-P140| F   | 50  | M2   | +    | Complex              | WT   | WT   |
| A10-P128| M  | 77  | M2   | +    | Complex              | ITD  | WT   |
| A11-P115| F  | 87  | M0   | +    | del 5                | WT   | WT   |
| A12-P107| M  | 73  | M2   | +    | Monosomal            | ITD  | WT   |
| A13-P123| M  | 81  | M2   | -    | -7                   | WT   | WT   |
| A14-P124| M  | 76  | M5   | +    | del 12, -7           | WT   | WT   |
| A15-P129| M  | 63  | M5   | +    | -7                   | WT   | WT   |
|        |     |     |      |      | Low-risk patients, i.e. favorable genetic abnormalities |      |      |
| F1-P110| F   | 67  | M4   | +    | t(16;16), +22        | -    | -    |
| F2-P116| M   | 36  | M5   | +    | inv16, +8, +22       | ITD  | WT   |
| F3-P139| M   | 66  | M5   | +    | t(16;16)             | WT   | WT   |
| F4-P141| M   | 79  | M2   | -    | inv16, del 7         | WT   | WT   |
| F5-P127| M   | 41  | M1   | +    | t(8;21), del 9, -3, -20, -22 | WT | WT   |
| F6-P131| F   | 33  | M1   | +    | t(8;21)              | WT   | WT   |
| F7-P137| F   | 74  | M4   | +    | t(8;21)              | ITD  | WT   |
| F8-P144| F   | 66  | M4   | +    | t(8;21)              | WT   | WT   |
| F9-P154| M   | 47  | M4   | -    | t(8;21)              | WT   | WT   |
| F10-P101| M  | 50  | M2   | -    | Normal                | WT   | INS  |
| F11-P118| F  | 61  | M5   | -    | Normal                | WT   | INS  |
| F12-P120| F  | 68  | M5   | -    | Normal                | WT   | INS  |
| F13-P125| M  | 64  | M5   | -    | Normal                | WT   | INS  |
| F14-P138| M  | 65  | M4   | -    | Normal                | WT   | INS  |
| F15-P143| M  | 64  | M1   | +    | Normal                | WT   | INS  |
| F16-P153| F  | 70  | M4   | +    | Normal                | WT   | INS  |
| F17-P155\(^3\)| F  | 71  | M0   | -    | Normal                | ITD\(^{low}\) | INS  |
| F18-P142\(^4\)| M  | 33  | M2   | +    | Normal                | WT   | WT   |

The table presents individually patient characteristics (sex, gender), morphological (FAB classification) and molecular signs of differentiation (CD34 expression), karyotype and FLT3/NPM1 mutational status\(^1\).

\(^1\)Abbreviations: FAB, French-American-British; INS, a 4 bp-insertion/duplication; ITD, internal tandem duplication; WT, wild-type; -, not determined.

\(^2\)Defined as ≥ 3 cytogenetic abnormalities.

\(^3\)The patient had a low ITD ratio and could therefore be classified as having a favorable prognosis. He was initially classified as ITD negative but later reclassified based on a new analysis.

\(^4\)This patient has CEBPA mutation.
Supplementary Table 2. Patient treatment and survival.

| ID       | Treatment                                                                 | Survival (months) |
|----------|---------------------------------------------------------------------------|-------------------|
| A1-P105  | Best supportive care                                                      | <1                |
| A2-P112  | AML-stabilizing therapy based on ATRA and valproic acid                    | 3                 |
| A3-P114  | AML-stabilizing therapy based on ATRA and valproic acid                    | 13                |
| A4-P117  | Best supportive care                                                      | 3                 |
| A5-P122  | AML-stabilizing therapy based on ATRA and valproic acid                    | 5                 |
| A6-P130  | Valproic acid plus hydroxyurea                                            | 3                 |
| A7-P133  | Best supportive care                                                      | <1                |
| A8-P134  | AML-stabilizing therapy based on ATRA and valproic acid                    | 1                 |
| A9-P140  | Intensive chemotherapy followed by allogeneic SCT                          | >46²              |
| A10-P128 | Best supportive care                                                      | <1                |
| A11-P115 | ATRA, valproic acid, low-dose cytarabine                                  | <1                |
| A12-P107 | Best supportive care                                                      | 2                 |
| A13-P123 | ATRA, valproic acid, low-dose cytarabine                                  | 16                |
| A14-P124 | Valproic acid plus hydroxyurea                                            | 6                 |
| A15-P129 | Best supportive care                                                      | 6                 |

**High risk patients, i.e. adverse cytogenetic abnormalities**

| ID       | Treatment                                                                 | Survival (months) |
|----------|---------------------------------------------------------------------------|-------------------|
| F1-P110  | Best supportive care                                                      | <1                |
| F2-P116  | Death from acute GVHD after allogeneic SCT in second CR                   | 25                |
| F3-P139  | ATRA, valproic acid, low-dose cytarabine                                  | <1                |
| F4-P141  | Valproic acid plus hydroxyurea                                            | 3                 |
| F5-P127  | Lost from follow-up                                                      | -                 |
| F6-P131  | Intensive chemotherapy followed by autologous SCT                          | >56               |
| F7-P137  | Azacitidine                                                               | 3                 |
| F8-P144  | Intensive induction and consolidation chemotherapy                          | >38               |
| F9-P154  | High-dose chemotherapy                                                    | >144              |
| F10-P101 | One cycle of intensive induction therapy with CR, no further chemotherapy due to severe toxicity | 28                |
| F11-P118 | Intensive induction therapy with CR, toxic death during consolidation     | 2                 |
| F12-P120 | Death from hyperleukocytosis                                              | <1                |
| F13-P125 | Intensive induction with CR, toxic death during consolidation therapy     | 2                 |
| F14-P138 | Intensive chemotherapy followed by autologous SCT, non-relapse death       | 14                |
| F15-P143 | Intensive induction with CR, toxic death during consolidation chemotherapy | 2                 |
| F16-P153 | AML-stabilizing therapy based on ATRA and valproic acid                   | 2                 |
| F17-P155 | Best supportive care                                                      | 2                 |
| F18-P142 | Intensive chemotherapy followed by autologous SCT                          | >44               |

**Low risk patients, i.e. favorable genetic abnormalities**

1³Abbreviations: ATRA, all-trans retinoic acid; CR, complete transmission; GVHD, Graft versus host disease; SCT: stem cell transplantation.

²The sign > means that the patient is still alive without relapse.
Supplementary Table 3. Classification of differentially expressed proteins and phosphorylated phosphoproteins found in the comparative studies between nine elderly low-risk and nine younger low-risk patients based on hallmarks of aging as explained in previous publications [1–3].

| Classification | Genomic stability, DNA repair | Mitosis, cell cycle | Epigenetics, chromatin, transcription, RNA splicing, ribosome | Protein homeostasis, metabolism, protein modification | Mitochondria, metabolism | Cytoskeleton, actin polarization | Intracellular ER/Golgi trafficking | Intracellular signaling | Extracellular secretion | Membrane structure | Tumor suppressor | Regulation of senescence | Regulation of apoptosis |
|----------------|-------------------------------|--------------------|-------------------------------------------------------------|-------------------------------------------------|-----------------------------|--------------------------------|-------------------------------|-------------------------|-----------------------------|-------------------|----------------|-------------------|-------------------------|
| APTX           | CDC27                         | CHD2               | ASPH                                                        | ALDH2                                           | CAP1                         | KIAA1279                       | GIT1                          | NENF                    | PTDSS1                      | PTPLAD2          | CAAP1          |                   |
| CAAP1          | KIAA1279                      | MARS2              | BAG2                                                        | COX6A1                                         | GIT1                         | NENF                           | SKAP2                         |                         |                             |                  |                |                   |
| NME3           | NUMB                          | RPS6KA4            | CDC27                                                       | KIAA1279                                       | PDP1                         | STX7                           | PDF                           |                         |                             |                  |                |                   |
| POLB           | WARS2                         |                    | MARS2                                                       | NME3                                           | PTDPLAD2                     | NEX2                           | PDF                           |                         |                             |                  |                |                   |
|                  |                                |                    |                                                             | NUMB                                           | PTP1                         | STX7                           | PDF                           |                         |                             |                  |                |                   |
| Pattern of altered protein level in low-risk patients | | | | | | | | | | | | | |
| RMI1           | CBX1                          | ARID1A             | DTNB1                                                       | ARID1A                                         | BIN1                         | DOCK5                          | LILRB3                        | BIN1                    | RERE                         |                  |                |                   |
| TOX4           | HECA                          | AHNK               |                                                             | FAM21C                                         | REPS1                        | FAM65B                         |                             |                         |                             |                  |                |                   |
| TP53BP1        | TMPO                          |                    |                                                             | WPB1                                           |                             |                                |                             |                         |                             |                  |                |                   |
| Pattern of increased phosphorylation in elderly low-risk patients | | | | | | | | | | | | | |
| LIG1           | CDK1                          | AATF               | ATAD2                                                       | IGF2BP1                                        | IGF2BP1                      | AATF                           | CDK2                          |                       |                             |                  |                |                   |
| CDK2           | ATAD2                         | BCLAF1             | ESY2                                                        | SCRI1B                                         | SCRI1B                       | CDK2                           | IGF2BP1                      |                       |                             |                  |                |                   |
| ESCO2          | BCLAF1                        | EEF2              | FOXK2                                                       | PCYT1B                                         |                             |                                |                             |                       |                             |                  |                |                   |
| FAM83H         | CHF1A                         | HSP90AB1           | NPM1                                                        |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| FOXK2          | CHD4                          | NPM1              | POLA2                                                       |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| GSG2           | CHD9                          | POLA2             |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| INCENP         | CNP                           | PPI6R3            |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| RB1            | EEF3F                         |                                 |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| HIST1H1D       |                                |                                 |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| IGF2BP1        |                                |                                 |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| ING5           |                                |                                 |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| KMT2A          |                                |                                 |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| NPM1           |                                |                                 |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| PPI6G          |                                |                                 |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| PRPF40A        |                                |                                 |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| RPRD2          |                                |                                 |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| RR1B           |                                |                                 |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| RR3B           |                                |                                 |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| SRRM1          |                                |                                 |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| SRRM2          |                                |                                 |                                 |                                 |                             |                                |                             |                       |                             |                  |                |                   |
| N2             | 8                             | 14                 | 43                                                          | 18                                            | 14                           | 11                             | 7                             | 2                       | 2                            | 8                | 1               | 6                 |

The table is based on information from the Gene database and selected references are from the PubMed database as described more in detail in Supplementary Tables 4–6. Abbreviations: ER, endoplasmic reticulum; N, number of proteins.