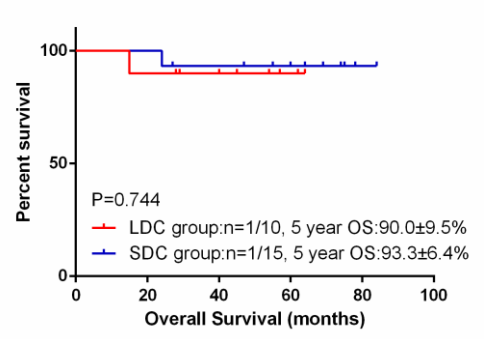
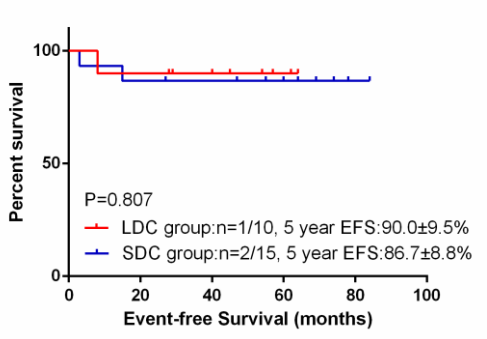
Supplemental Figure Legends

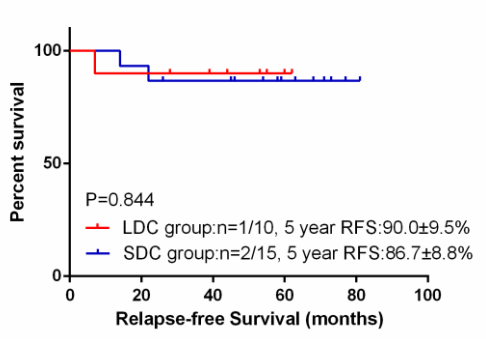
Supplemental Figure 1. **Outcome according to risk classification and treatment group.** Abbreviations: LDC, low-dose chemotherapy; SDC, standard-dose chemotherapy; OS, overall survival; EFS, event-free survival; RFS, relapse-free survival.

Supplemental Figure 1.

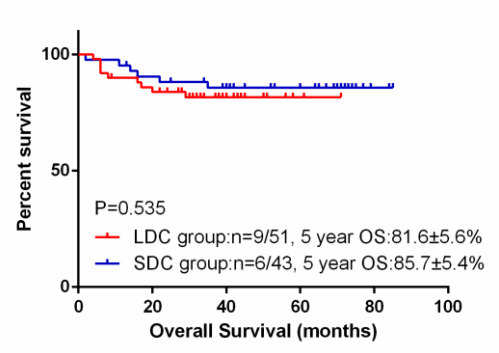
Definitive low risk

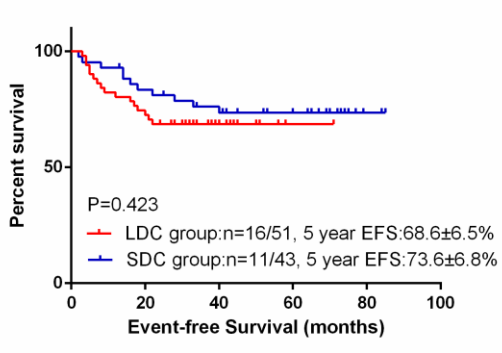


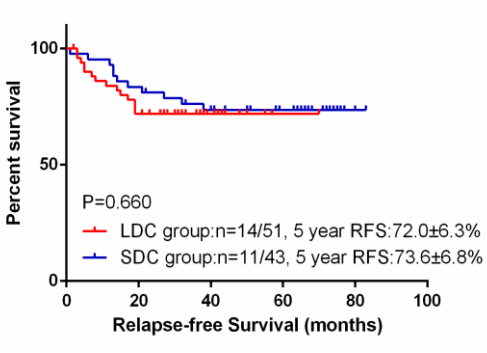




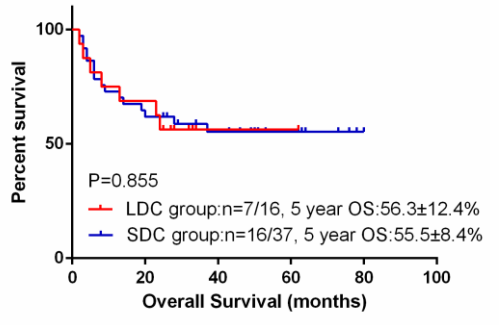
Definitive intermediate risk

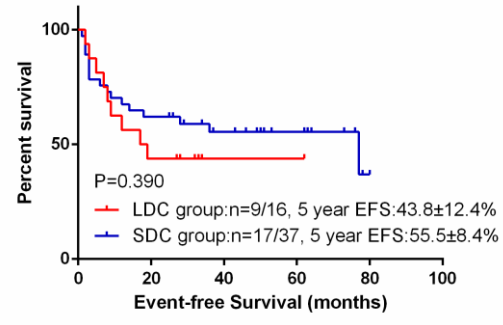


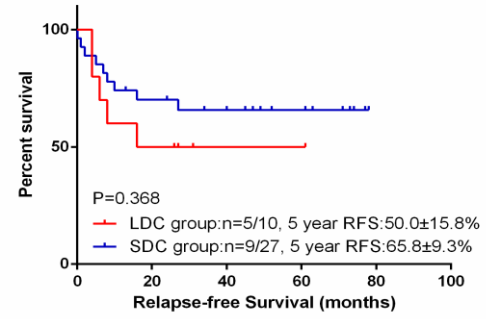




Definitive high risk







Supplemental Table 1. Provisional risk classification

Risk classification	Criteria
Low risk	1. t(8;21)(q22;q22)/*RUNX1–RUNX1T1*, inv(16)(p13.1q22), t(16;16)(p13.1;q22)/*CBFB-MYH11*, t(1;11)(q21;q23)/*MLL–MLLT11*(*AF1Q*), **or** **2.** Normal karyotype with *NPM1* mutations, *CEBPα* biallelic mutations, **and** **3.** Absence of numerical changes (-X, -Y) or mutations in AML-related genes (*CBL, NRAS, c-KIT, PTPN11, FLT3*) **and** 4. Absence of extramedullary involvement or myeloid sarcoma.
Intermediate risk	1. Low-risk cases with WBC ≥ 100×10^9/L, numerical or structural karyotype abnormalities, extramedullary involvement (CNS, testicles, skin), or myeloid sarcoma; 2. t(9;11) (p22;q23)/*MLL–MLLT3(AF9)*; 3. Cases that do not meet the low-risk or high-risk criteria.
High risk	1. No low-risk cases with WBC ≥ 100×10^9/L or myeloid sarcoma; 2. Specific gene rearrangements: t(5;11)(q35;p15.5)/*NUP98–NSD1*, t(6;11)(q27;q23)/*KMT2A–AFDN(AF6)*, t(4;11)(q21;q23)/*KMT2A–AFF1(AF4)*, t(10;11)(p12;q23)/*KMT2A–MLLT10(AF10)*, t(6;9)(p23;q34)/*DEK–NUP214,* t(7;12)(q36;p13)/*MNX1–ETV6*, t(9;22)(q34;q11.2)/*BCR–ABL*, t(8;16) (p11;p13)/*KAT6A–CREBBP*, t(16;21) (q24;q22)/*RUNX1–CBFA2T3*, inv(16)(p13.3q24.3)/*CBFA2T3–GLIS2*, t(11;12)(p15;p13)/*NUP98–KDM5A*, t(7;11)(p15.2;p15.4)/*NUP98–HOX13*, inv(3)(q21.3q26.2), t(3;3)(q21.3q26.2)/*RPN1–MECOM*, or *FLT3*-ITD; mutations in *RUNX1*, *TP53*, and *ASXL1*; *KMT2A* dup; or other *KMT2A* rearrangements; multidrug-resistant (MRD-1) AML; 3. Complex karyotype (harboring 3 or more acquired chromosome aberrations, including translocation); 4. AML-M6; 5. t-AML

Supplemental Table 2 and Supplemental Table 3 appear online as separate Excel files.

Supplemental Table 4. Univariate analysis of overall survival and event-free survival for the whole cohort

Factor	n (%)	Overall survival			Event-free survival		
		HR	95% CI	*P*	HR	95% CI	*P*
Age, years							
1-10	129 (70.5)	Reference			Reference		
<1	10 (5.5)	1.864	0.658-5.283	0.241	1.170	0.420-3.259	0.763
>10	44 (24.0)	1.419	0.755-2.667	0.278	1.186	0.680-2.070	0.547
Sex							
Male	106 (57.9)	Reference			Reference		
Female	77 (42.1)	1.168	0.665-2.051	0.589	1.009	0.621-1.639	0.972
WBC, $\times 10^9$/L							
<100	152 (83.1)	Reference			Reference		
≥100	31 (16.9)	2.241	1.205-4.167	**0.011**	1.421	0.788-2.563	0.242
FAB subtype							
M1/M2	81 (44.3)	Reference			Reference		

M4/M5	80 (43.7)	1.977	1.032-3.787	**0.040**	1.465	0.863-2.489	0.158
M7	8 (4.4)	2.130	0.612-7.414	0.235	1.222	0.368-4.060	0.743
Other	14 (7.6)	2.860	1.098-7.451	**0.031**	2.450	1.098-5.464	**0.029**
Definitive risk							
Low risk	25 (14.5)	Reference			Reference		
Intermediate risk	94 (54.7)	2.165	0.495-9.469	0.305	2.573	0.781-8.484	0.120
High risk	53 (30.8)	7.291	1.717-30.969	**0.007**	5.420	1.639-17.925	**0.006**
Treatment group							
SDC/SDC	96 (53.6)	Reference			Reference		
LDC/SDC	25 (14.0)	1.703	0.791-3.665	0.174	2.004	1.025-3.917	**0.042**
LDC/LDC	58 (32.4)	0.919	0.468-1.807	0.808	1.132	0.642-1.994	0.669
Omacetaxine mepesuccinate							
No	112 (63.6)	Reference			Reference		
Yes	64 (36.4)	0.748	0.390-1.437	0.384	0.714	0.410-1.242	0.233
HSCT							
No	97 (53.0)	Reference			Reference		

Yes	86 (47.0)	0.423	0.230-0.777	**0.006**	0.704	0.433-1.145	0.157

Abbreviations: CI, confidence interval ; FAB, French–American–British; HR, hazard ratio; HSCT, hematopoietic stem cell transplantation; LDC, low-dose chemotherapy; SDC, standard-dose chemotherapy; WBC, white blood cell..

Selected data on 46 study patients have been reported previously.[20]

Supplemental Table 5. Multivariate Cox regression analysis of survival for patients with initial WBC count < 100 × 10^9/L

Variables	n (%)	Overall survival			Event-free survival		
		HR	95% CI	*P*	HR	95% CI	*P*
Treatment group							
SDC/SDC	72 (49.0)	Reference			Reference		
LDC/LDC	53 (36.0)	1.595	0.705-3.608	0.262	1.539	0.802-2.951	0.195
LDC/SDC	22 (15.0)	1.698	0.636-4.534	0.291	1.819	0.806-4.106	0.150
Initial risk							
Low risk	25 (17.0)	Reference			Reference		
Intermediate risk	93 (63.3)	3.281	0.753-14.302	0.114	3.434	1.039-11.349	**0.043**
High risk	29 (19.7)	9.273	1.956-43.973	**0.005**	5.672	1.559-20.636	**0.008**
HSCT							
No	77 (52.4)	Reference			Reference		
Yes	70 (47.6)	0.252	0.111-0.576	**0.001**	0.556	0.305-1.012	0.055

Abbreviations: CI, confidence interval; HR, hazard ratio; HSCT, hematopoietic stem cell transplantation; LDC, low-dose chemotherapy; SDC, standard-dose chemotherapy; WBC, white blood cell.

Supplemental Table 6. Selected adverse events observed in remission induction I and II and in consolidation I

Adverse events	Remission induction I				Remission induction II				Consolidation I			
	LDC (N = 83*) n (%)	**SDC (N = 100) n (%)**	**Total (N = 183) n (%)**	***P*** †	**LDC (N = 58) n (%)**	**SDC (N = 118) n (%)**	**Total (N = 176) n (%)**	***P*** †	**LDC (N = 54) n (%)**	**SDC (N = 97) n (%)**	**Total (N = 151) n (%)**	***P*** †
Platelet recovery, days												
Median	11	16	14	**<0.001**	3	7.5	4	**<0.001**	5	8	7	**0.005**
Range	0-30	3-33	0-33		0-23	0-37	0-37		0-25	0-34	0-34	
Days with neutropenia												
Median	12	20	17	**<0.001**	6.5	15	12	**<0.001**	13.5	16.0	14.0	**0.012**
Range	0-30	3-47	0-47		0-19	5-49	0-49		6-29	6-67	6-67	
Pneumonia												
No	57 (68.7)	54 (54.0)	111 (60.7)	**0.019**	56 (96.6)	95 (80.5)	151 (85.8)	**0.013**	40 (74.1)	77 (79.4)	117 (77.5)	0.756
Grade 1 or 2	6 (7.2)	3 (3.0)	9 (4.9)		0 (0.0)	2 (1.7)	2 (1.1)		0 (0.0)	1 (1.0)	1 (0.7)	
Grade 3 or 4	20 (24.1)	43 (43.0)	63 (34.4)		2 (3.4)	20 (17.0)	22 (12.5)		14 (25.9)	18 (18.6)	32 (21.1)	
Grade 5	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	1 (0.8)	1 (0.6)		0 (0.0)	1 (1.0)	1 (0.7)	
Febrile neutropenia												
No	32 (38.6)	9 (9.0)	41 (22.4)	**<0.001**	47 (81.0)	13 (11.0)	60 (34.1)	**<0.001**	4 (7.4)	11 (11.4)	15 (9.9)	0.727
Grade 1 or 2	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	
Grade 3 or 4	51 (61.4)	91 (91.0)	142 (77.6)		11 (19.0)	104 (88.2)	115 (65.3)		50 (92.6)	85 (87.6)	135 (89.4)	
Grade 5	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	1 (0.8)	1 (0.6)		0 (0.0)	1 (1.0)	1 (0.7)	
Sepsis												

No	81 (97.6)	95 (95.0)	176 (96.2)	0.459	55 (94.8)	105 (89.0)	160 (90.9)	0.270	44 (81.5)	69 (71.1)	113 (74.8)	0.350
Grade 1 or 2	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	
Grade 3 or 4	2 (2.4)	5 (5.0)	7 (3.8)		3 (5.2)	13 (11.0)	16 (9.1)		10 (18.5)	27 (27.9)	37 (24.5)	
Grade 5	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	1 (1.0)	1 (0.7)	
Bleeding												
No	81 (97.6)	88 (88.0)	169 (92.4)	**0.046**	58 (100.0)	113 (95.8)	171 (97.2)	0.400	54 (100.0)	97 (100.0)	151 (100.0)	--
Grade 1 or 2	0 (0.0)	6 (6.0)	6 (3.3)		0 (0.0)	4 (3.4)	4 (2.3)		0 (0.0)	0 (0.0)	0 (0.0)	
Grade 3 or 4	2 (2.4)	5 (5.0)	7 (3.8)		0 (0.0)	1 (0.8)	1 (0.5)		0 (0.0)	0 (0.0)	0 (0.0)	
Grade 5	0 (0.0)	1 (1.0)	1 (5.5)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	
Oral mucositis												
No	82 (98.8)	89 (89.0)	171 (93.4)	**0.007**	58 (100.0)	115 (97.5)	173 (98.3)	0.552	54 (100.0)	95 (97.9)	149 (98.7)	0.537
Grade 1 or 2	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0(0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	
Grade 3 or 4	1 (1.2)	11 (11.0)	12 (6.6)		0 (0.0)	3 (2.5)	3 (1.7)		0 (0.0)	2 (2.1)	2 (1.3)	
Perianal rectal infection												
No	83 (100.0)	98 (98.0)	181 (98.9)	0.502	58 (100.0)	109 (92.4)	167 (94.9)	**0.031**	54 (100.0)	93 (95.9)	147 (97.4)	0.297
Grade 1 or 2	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	
Grade 3 or 4	0 (0.0)	2 (2.0)	2 (1.1)		0 (0.0)	9 (7.6)	9 (5.1)		0 (0.0)	4 (4.1)	4 (2.6)	
Gastrointestinal infection												
No	83 (100.0)	100 (100.0)	183 (100.0)	--	58 (100.0)	111 (94.1)	169 (96.0)	0.097	54 (100.0)	97 (100.0)	151 (100.0)	--
Grade 1 or 2	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	
Grade 3 or 4	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	7 (5.9)	7 (4.0)		0 (0.0)	0 (0.0)	0 (0.0)	

Abbreviations: LDC, low-dose chemotherapy; SDC, standard-dose chemotherapy.

* Selected data on 46 study patients have been previously reported.[20]

† The Mann–Whitney U test was used for continuous variables; Fisher's exact test was used for categorical variables with 2×2 charts; Monte Carlo analysis was used for categorical variables with N×2 charts.

Supplemental Table 7. Blood products usage and cost of remission induction I and II and consolidation

	Remission induction I				Remission induction II				Consolidation I			
Treatment	**LDC (N = 83*)**	**SDC (N = 100)**	**Total (N = 183)**	***P***	**LDC (N = 58)**	**SDC (N = 118)**	**Total (N = 176)**	***P***	**LDC (N = 54)**	**SDC (N = 97)**	**Total (N = 151)**	***P***
PRBCs, U												
Median	3	5	4	**<0.001**	0	3	2	**<0.001**	1	2	2	**<0.001**
Range	0-12	1-24	0-24		0-12	0-14	0-14		0-6	0-12	0-12	
PLTs, IU												
Median	30	40	30	**0.001**	10	20	20	**<0.001**	20	20	20	0.096
Range	0-90	10-150	0-150		0-50	0-90	0-90		0-80	5-70	0-80	
Cost of transfusions, $												
Median	723	973	825	**<0.001**	210	569	450	**<0.001**	420	600	540	**0.011**
Range	0.0-2,325	300-3,870	0.0-3,870		0.0-1,286	0.0-3,804	0.0-3,804		0.0-1,901	105-1,631	0.0-1,910	
Cost of antibiotics, $												
Median	1,350	2,710	2,162	**<0.001**	0.0	1,573	868	**<0.001**	1,259	1,510	1,413	0.485
Range	0.0-1,726	0.0-13,700	0.0-1,726		0.0-3,973	0.0-11,047	0.0-11,047		0.0-8,445	0.0-9,310	0.0-9,310	
Total cost, $†												
Median	9,043	10,731	9,805	0.082	2,369	5,398	4,369	**<0.001**	5,574	5,478	5,500	0.930
Range	4,016-33,746	958-28,503	958-33,746		990-15,769	1,203-22,478	990-22,478		1,886-22,596	776-20,247	776-22,596	

Abbreviations: LDC, low-dose chemotherapy; PRBCs, packed red blood cells; PLTs, platelets; SDC, standard-dose chemotherapy.

* Selected data on 46 study patients have been previously reported.[20]

†Total cost includes chemotherapy, transfusions of blood and platelets, antibiotics, various tests, and inpatient consumptions.

Supplemental Table 8. Selected supportive care measures

Pediatric Oncology Unit	Characteristics
Hospital rooms for pediatric hematology	The pediatric hematology unit has 24 rooms without air filters or controlled ventilation pressure. There is a sink for handwashing and a dedicated bathroom for the patients. The number of patients per room varies from 1 to 3, and one parent for each patient is allowed.
Clinical laboratory	Routine ancillary tests are available 24 hours per day/7 days a week. Time to return results is as follows: 1. CBC and electrolytes—1 hour 2. Biochemical panel—2 to 4 hours 3. Microbiology—8 to 12 hours
Hospital Infection Control	A hospital infection control committee monitors the entire hospital's infection rates and makes recommendations.
Nursing	Dedicated pediatric oncology trained nurses or general pediatric nurses are available. A ratio of nurses to patients of 1:3 is maintained, including on weekends.
Prophylactic antibiotics and antifungals	Prophylactic antibiotics are not used. Fluconazole is used during periods of neutropenia.
Central line catheters	A peripheral inserted central venous catheter, port-cath, or tunneled central venous catheter is selected according to the patients' age, physical status, and type of therapy. A nurse provides routine care according to the requirements of each central line catheter.
Patient and family education	Education for patients and families by nurses and physicians is started at the time of admission. The educational content includes nutritional guidelines during chemotherapy, hygiene, and infection prevention and detection. Parents are instructed to report immediately to the hospital in cases of abnormal temperature or signs of bleeding.
Fever and neutropenia	All patients with AML start antimicrobial during neutropenia if they develop fever, oral mucositis, skin infection, diarrhea, or hemodynamic instability. If the ANC is less than 0.5×10^9/L, meropenem or imipenem is used first. If the patient does not improve within 48 hours, vancomycin is started. Teicoplanin or linezolid is administered if patients do not tolerate vancomycin. The antibiotic and antifungal coverage is modified according to the results of microbiology tests. Caspofungin, fluconazole, and voriconazole are available. If the ANC is more than 0.5×10^9/L, a second- or third-generation cephalosporin is used as a first antibiotic.
Physician coverage	The unit is staffed by two teams, each consisting of one senior physician coordinating the treatment with two junior pediatric hematologists, undergraduate medical students, and residents in training.

Intensive care unit	A general pediatric intensive care unit is available. Pediatric acute care attendings and the primary senior hematologist coordinate the care.
Blood products	Platelet concentrate and packed red cells are transfused for patients with a platelet count less than 20×10^9/L and a hemoglobin level less than 60 g/L, respectively. The blood products are leukoreduced but are not irradiated (except during HSCT).
Housing for families	If the family's home is more than 2 driving hours from the hospital, parents are instructed to rent a house near the hospital.
Other hospitals in the community	Depending on the distance between the hospital and the patient’s home, the primary physician on service determines whether to refer a patient with fever to another local hospital. The primary physician on service monitors the progress of the patients admitted to the treating hospitals.