

Outcome and Prognostic Factors for *ETV6/RUNX1* Positive Pediatric Acute Lymphoblastic Leukemia Treated at a Single Institution in Korea

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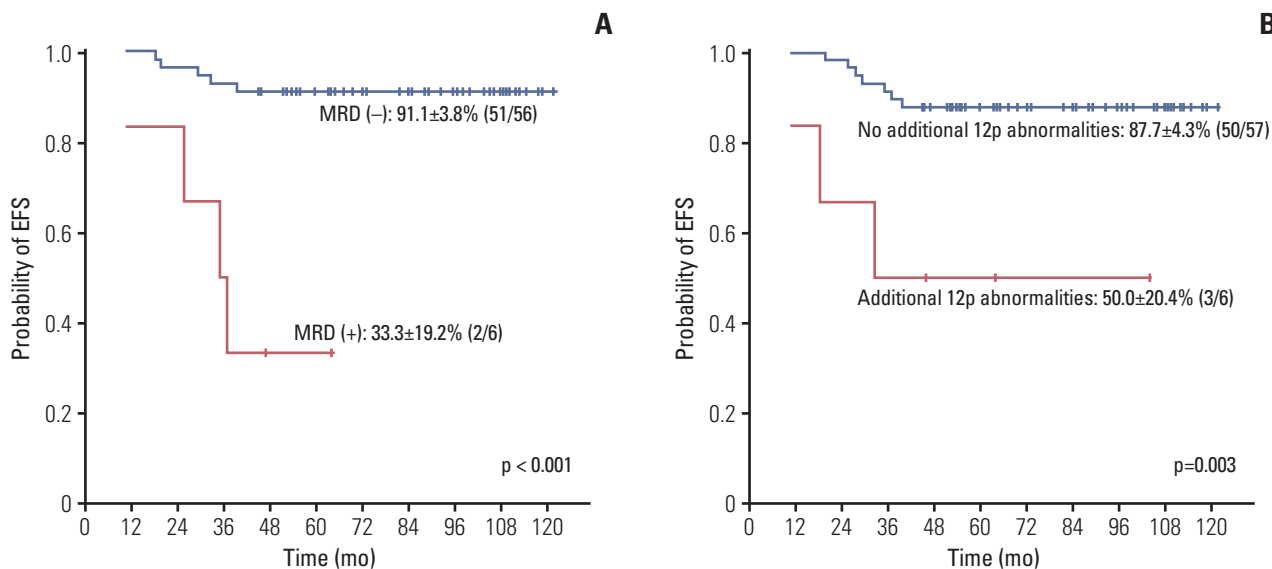
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Supplementary Data

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Supplementary Fig. S1. (A) Event-free survival (EFS) according to presence of minimal residual disease (MRD) at end of remission induction: MRD (-) 91.1±3.8% (51/56), MRD (+) 33.3±19.2% (2/6). (B) EFS according to presence of additional 12p structural abnormalities (translocations or inversions): without additional 12p structural abnormalities 87.7±4.3% (50/57), with additional 12p structural abnormalities 50.0±20.4% (3/6).

Supplementary Table 1. Risk group classification of ALL

Risk group	Criteria
Low	All of the following: Age ≥ 1 and < 10 years old Initial WBC count < 50,000/mm ³ Trisomies of 4, 10, 17 or <i>ETV6/RUNX1</i> (+)
Standard	As above, except lack of trisomies of 4, 10, 17 or <i>ETV6/RUNX1</i> (+)
High	Any of the following: Age ≥ 10 and < 15 years old Initial WBC count ≥ 50,000/mm ³ and < 100,000/mm ³ Initial CNS or testicular involvement Precursor B cell ALL with poor prephase steroid response ^{a)} <i>E2A/PBX1</i> (+) <i>MLL</i> rearrangement MRD (+) at end of remission induction T cell ALL with good prephase steroid response
Very high	Any of the following: Age ≥ 15 years old Initial WBC count ≥ 100,000/mm ³ <i>BCR/ABL1</i> (+) ALL Infant ALL Hypodiploidy with < 45 chromosomes T cell ALL with poor prephase steroid response CR not achieved after first remission induction

ALL, acute lymphoblastic leukemia; WBC, white blood cell; CNS, central nervous system; MRD, minimal residual disease; CR, complete remission. ^{a)}Poor prephase steroid response indicates a peripheral blast count ≥ 1,000/mm³ after 7 days of steroid treatment.

Supplementary Table 2. Remission induction and consolidation

Drug	Dose	Day
Prephase		
Prednisolone (PO) ^{a)}	60 mg/m ² (max. 80 mg)	1-7
Methotrexate/Cytarabine/Hydrocortisone (IT)	By age ^{b)}	1
Remission induction		
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	1, 8, 15, 22
Daunorubicin (IV)	45 mg/m ²	1
L-asparaginase (IM)	6,000 U/m ² (max. 10,000 U)	2, 4, 6, 9, 11, 13, 16, 18, 20
Prednisolone (PO)	60 mg/m ² (max. 80 mg)	1-21
Methotrexate (IT)	By age ^{c)}	1, 22
Consolidation		
Cyclophosphamide (IV)	1,000 mg/m ²	1, 29
Cytarabine (IV)	100 mg/m ²	1-5, 15-19, 29-33, 43-47
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	15, 22, 43, 50
Prednisolone (PO)	45 mg/m ² (max. 60 mg)	22-26, 50-54
6-Mercaptopurine (PO)	60 mg/m ²	1-7, 29-35
Methotrexate (IT)	By age ^{c)}	1, 15, 29, 43

PO, per os; IT, intrathecal; IV, intravenous; IM, intramuscular. ^{a)}For patients diagnosed and treated from January 2009 onwards, prednisolone was used for treatment. However, for patients diagnosed from January 2005 to December 2008, dexamethasone was used at a dose of 8 mg/m²/day PO (max. 10 mg/day), ^{b)}Age-adjusted doses of triple intrathecal chemotherapy. Methotrexate: 6 mg (< 1 year), 7.5 mg (≥ 1 and < 2 years), 10 mg (≥ 2 and < 3 years), 12.5 mg (≥ 3 years); Cytarabine: 12 mg (< 1 year), 15 mg (≥ 1 and < 2 years), 20 mg (≥ 2 and < 3 years), 25 mg (≥ 3 years); Hydrocortisone: 12 mg (< 1 year), 15 mg (≥ 1 and < 2 years), 20 mg (≥ 2 and < 3 years), 25 mg (≥ 3 years), ^{c)}Age-adjusted doses of intrathecal methotrexate: 6 mg (< 1 year), 7.5 mg (≥ 1 and < 2 years), 10 mg (≥ 2 and < 3 years), 12.5 mg (≥ 3 years).

Supplementary Table 3. Post-consolidation: low risk

Drug	Dose	Day
Interim maintenance		
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	1, 15
Methotrexate (IV)	5 g/m ²	1, 15
6-Mercaptopurine (PO)	60 mg/m ²	29-77
Methotrexate (IT)	By age ^{a)}	1
Delayed intensification		
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	1, 15, 29, 43
Daunorubicin (IV)	30 mg/m ²	1, 29
Cytarabine (IV)	100 mg/m ²	1-5, 29-33
Cyclophosphamide (IV)	1,200 mg/m ²	15, 43
L-asparaginase (IM)	6,000 U/m ² (max. 10,000 U)	16, 18, 20, 44, 46, 48
Prednisolone (PO)	45 mg/m ² (max. 60 mg)	1-5, 15-19, 29-33, 43-47
Methotrexate (IT)	By age ^{a)}	1, 29

IV, intravenous; PO, per os; IT, intrathecal; IM, intramuscular. ^{a)}Age-adjusted doses of intrathecal methotrexate: 6 mg (< 1 year), 7.5 mg (≥ 1 and < 2 years), 10 mg (≥ 2 and < 3 years), 12.5 mg (≥ 3 years).

Supplementary Table 4. Post-consolidation: standard risk

Drug	Dose	Day
Interim maintenance		
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	1, 15, 29
Methotrexate (IV)	5 g/m ²	1, 15, 29
6-Mercaptopurine (PO)	60 mg/m ²	43-77
Methotrexate (IT)	By age ^{a)}	1, 15, 29
Delayed intensification		
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	1, 15, 29, 43
Daunorubicin (IV)	30 mg/m ²	1, 15, 29, 43
Cytarabine (IV)	100 mg/m ²	1-5, 29-33
Cyclophosphamide (IV)	1,200 mg/m ²	15, 43
L-asparaginase (IM)	6,000 U/m ² (max. 10,000 U)	16, 18, 20, 44, 46, 48
Prednisolone (PO)	45 mg/m ² (max. 60 mg)	1-5, 15-19, 29-33, 43-47
Methotrexate (IT)	By age ^{a)}	1, 29

IV, intravenous; PO, per os; IT, intrathecal; IM, intramuscular. ^{a)}Age-adjusted doses of intrathecal methotrexate: 6 mg (< 1 year), 7.5 mg (≥ 1 and < 2 years), 10 mg (≥ 2 and < 3 years), 12.5 mg (≥ 3 years).

Supplementary Table 5. Post-consolidation: high risk

Drug	Dose	Day
Interim maintenance		
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	1, 15, 29
Methotrexate (IV)	5 g/m ²	1, 15, 29
HD cytarabine (IV)	3 g/m ² (q 12 hours)	43, 44
L-asparaginase (IM)	6,000 U/m ² (max. 10,000 U)	44
6-Mercaptopurine (PO)	60 mg/m ²	64-77
Methotrexate (IT)	By age ^{a)}	1, 15, 29, 43
Delayed intensification		
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	1, 15, 29, 43
Daunorubicin (IV)	30 mg/m ²	1, 15, 29, 43
Cytarabine (IV)	100 mg/m ²	1-5, 29-33
Cyclophosphamide (IV)	1,200 mg/m ²	15, 43
L-asparaginase (IM)	6,000 U/m ² (max. 10,000 U)	16, 18, 20, 44, 46, 48
Prednisolone (PO)	45 mg/m ² (max. 60 mg)	1-5, 15-19, 29-33, 43-47
Methotrexate (IT)	By age ^{a)}	1, 29
Interim maintenance-II		
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	1, 22
Methotrexate (IV)	500 mg/m ²	1, 22
Prednisolone (PO)	45 mg/m ² (max. 60 mg)	1-5, 22-26
6-Mercaptopurine (PO)	60 mg/m ²	1-42
Methotrexate (IT)	By age ^{a)}	1, 22
Delayed intensification-II		
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	1, 15
Daunorubicin (IV)	30 mg/m ²	1, 15
Cytarabine (IV)	100 mg/m ²	1-5
Cyclophosphamide (IV)	1,200 mg/m ²	15
L-asparaginase (IM)	6,000 U/m ² (max. 10,000 U)	16, 18, 20, 30
Prednisolone (PO)	45 mg/m ² (max. 60 mg)	1-5, 15-19
HD cytarabine (IV)	3 g/m ² (q 12 hours)	29, 30
Methotrexate (IT)	By age ^{a)}	1, 29

IV, intravenous; HD, high dose; IM, intramuscular; PO, per os; IT, intrathecal. ^{a)}Age-adjusted doses of intrathecal methotrexate: 6 mg (< 1 year), 7.5 mg (≥ 1 and < 2 years), 10 mg (≥ 2 and < 3 years), 12.5 mg (≥ 3 years).

Supplementary Table 6. Post-consolidation: very high risk

Drug	Dose	Day
Interim maintenance		
HD cytarabine (IV)	3 g/m ² (q 12 hours)	1, 2, 50, 51
L-asparaginase (IM)	6,000 U/m ² (max. 10,000 U)	2, 51
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	22, 36
Methotrexate (IV)	5 g/m ²	22, 36
Methotrexate (IT)	By age ^{a)}	1, 22, 36, 50
Delayed intensification		
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	1, 15, 29, 43
Daunorubicin (IV)	30 mg/m ²	1, 15, 29, 43
Cytarabine (IV)	100 mg/m ²	1-5, 29-33
Cyclophosphamide (IV)	1,200 mg/m ²	15, 43
L-asparaginase (IM)	6,000 U/m ² (max. 10,000 U)	16, 18, 20, 44, 46, 48
Prednisolone (PO)	45 mg/m ² (max. 60 mg)	1-5, 15-19, 29-33, 43-47
Methotrexate (IT)	By age ^{a)}	1, 29
Interim maintenance-II		
HD cytarabine (IV)	3 g/m ² (q 12 hours)	1, 2, 50, 51
L-asparaginase (IM)	6,000 U/m ² (max. 10,000 U)	2, 51
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	22, 36
Methotrexate (IV)	5 g/m ²	22, 36
Methotrexate (IT)	By age ^{a)}	1, 22, 36, 50
Delayed intensification-II		
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	1, 15
Daunorubicin (IV)	30 mg/m ²	1, 15
Cytarabine (IV)	100 mg/m ²	1-5
Cyclophosphamide (IV)	1,200 mg/m ²	15
L-asparaginase (IM)	6,000 U/m ² (max. 10,000 U)	16, 18, 20, 30
Prednisolone (PO)	45 mg/m ² (max. 60 mg)	1-5, 15-19
HD cytarabine (IV)	3 g/m ² (q 12 hours)	29, 30
Methotrexate (IT)	By age ^{a)}	1, 29

HD, high dose; IV, intravenous; IM, intramuscular; PO, per os; IT, intrathecal. ^{a)}Age-adjusted doses of intrathecal methotrexate: 6 mg (< 1 year), 7.5 mg (≥ 1 and < 2 years), 10 mg (≥ 2 and < 3 years), 12.5 mg (≥ 3 years).

Supplementary Table 7. Maintenance treatment (for 96 weeks)^{a)}

Drug	Dose	Day
6-Mercaptopurine (PO)	60 mg/m ²	Daily
Methotrexate (PO)	25 mg/m ²	Weekly
Vincristine (IV)	1.5 mg/m ² (max. 2 mg)	Every 4 weeks
Prednisolone (PO)	45 mg/m ² (max. 60 mg) for 5 days	Every 4 weeks
Methotrexate (IV)	3 g/m ²	Every 12 weeks
Methotrexate (IT)	By age ³⁾	Every 12 weeks

PO, per os; IV, intravenous; IT, intrathecal; HD, high dose. ^{a)}Maintenance treatment begins and ends with high dose methotrexate (3 g/m² IV), vincristine (1.5 mg/m² IV), prednisolone (45 mg/m² PO for 5 days), and IT methotrexate. A total of nine courses of high-dose methotrexate (HD-methotrexate) are administered during maintenance treatment. Oral methotrexate (25 mg/m² weekly) is omitted during the week of HD-methotrexate treatment. The regimen of maintenance treatment is common for all risk groups.