Suplemental Digdital Content Table1. Drug Dosage and Schedules for ALL941/2000 Protocols

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|  | Regimen | Daily dose | Administration | Days |
| Induction phase |  |  |  |  |
| Ind-1 (VPLA) | Vincristine | 2 mg/m2 | IV | 1, 8, 15, 22 |
|  | Prednisolone | 60 mg/m3 | Oral | 1–28 |
|  | L-Asparaginase | 2,000 U/m2 | IV | 8–26 (3/w) |
|  | Doxorubicin | 25 mg/m3 | IV | 1 |
| Ind-2 (VPLA\_) Same as in Int-I except for Dox (25 mg/mg2 Å~3 at days 1, 18, 15) | | | | |
| Ind-3 (VPLA’ +EC) | Etoposide | 150 mg/m2 | IV | 22, 29, 36 |
|  | Cytarabine | 300 mg/m2×2 | IV | 22, 29, 36 |
| Intensification phase |  |  |  |  |
| lnt-1 | Pirarubicin | 20 mg/m2 | IV | 1 |
|  | Vincristine | 2 mg/m2 | IV | 1 |
|  | Prednisolone | 120 mg/m2 | Oral | 1–5 |
|  | 6-Mercaptopurine | 250 mg/m2 | Oral | 1–5 |
|  | Cyclophosphamide | 400 mg/m2 | IV | 15 |
|  | Cytarabine | 50 mg/m2×2 | IV | 15–18 |
|  | 6-Mercaptopurine | 125 mg/m2 | Oral | 15–19 |
|  | Methotrexate | 500 mg/m2 | IV | 29 |
|  | L-Asparaginase | 2,000 U/m2 | IV | 30, 31 |
| Int-2 Same as in Int-1 except for LASP (6,000 U/m2, weekly for 12 weeks) | | | | |
| lnt-3 (Int-2+EC) | Etoposide | 100 mg/m2 | IV | 43–45 |
|  | Cytarabine | 2 g/m2×2 | IV | 43–47 |
| CNS prophylaxis |  |  |  |  |
| TIT | Methotrexate | 12 mg/m2 | IT |  |
|  | Cytarabine IT | 30 mg/m2 | IT |  |
|  | Hydorocortisone | 50 mg/m2 | IT |  |
| Reinduction phase |  |  |  |  |
| Rc-1 (VPLA’’) | Vincristine | 2 mg/m2 | IV | 1, 8, 15, 22 |
|  | Prednisolone | 60 mg/m2 | Oral | 1–28 |
|  | L-Asparaginase | 2,000 U/m2 | IV | 1, 8, 15, 22, 29 |
|  | Pirarubicin | 25 mg/m2 | IV | 8, 15, 22 |
| Rc-2 (VPLA’’ +EC) | Etoposide | 150 mg/m2 | IV | 22, 29, 36 |
|  | Cytarabine | 300 mg/m2×2 | IV | 22, 29, 36 |
| Rc-3 (VPL+EC +M) | Etoposide | 300 mg/m2 | IV | 8, 22, 36 |
|  | Cytarabine | 300 mg/m2×2 | IV | 8, 22, 36 |
|  | Mitoxantrone | 10 mg/m2 | IV | 50, 57, 64 |
| Maintenance phase |  |  |  |  |
| M-l (VPMA-CCM-ML) | Pirarubicin | 20 mg/m2 | IV | 1 |
|  | Vincristine | 2 mg/m2 | IV | 1 |
|  | Prednisolone | 120 mg/m2 | Oral | 1–5 |
|  | 6-Morcaptopurine | 250 mg/m2 | Oral | 1–5 |
|  | Cyclophosphamide | 400 mg/m2 | IV | 15 |
|  | Cytarabine | 50 mg/m2×2 | IV | 15–18 |
|  | 6-Mcrcaptopurine | 125 mg/m2 | Oral | 15–19 |
|  | Methotrexate | 225 mg/m2 | IV | 28 |
|  | L-Asparaginase | 2,000 U/m2 | IV | 28 |
| M-2 (VPM-ML) | Vincristine | 2 mg/m2 | IV | 1–5 |
|  | Prednisolone | 120 mg/m2 | Oral | 1–5 |
|  | 6-Mercaptopurine | 250 mg/m2 | Oral | 1–5 |
|  | Methotrexate | 225 mg/m2 | IV | 14 |
|  | L-Asparaginase | 2,000 U/m2 | IV | 15 |
| M-3 (VPMA-ML) Same as in M-2 except for pirarubicin (20 mg/m2 at day 1) | | | |  |

IV, intravenous; IT, intrathecal.

Supplemental Digital Content 1 (Table 1.)

Treatment of ALL941/2000 comprised four phases: induction, intensification, reinduction, and maintenance. Induction therapy in the SR and HR groups included vincristine, PSL, L-asparaginase (LASP; Kyowa Hakko Kirin, Tokyo, Japan), and DOX. Etoposide and cytarabine were added to the induction regimen in the HHR group. After achieving complete remission, the patients received intensification therapy, which included the alternate use of eight drugs in three blocks at 2-week intervals. HR/HHR patients received reinduction therapy at week 14 followed by intensification therapy, which included weekly LASP administration until week 30. HHR patients with minimal residual disease (MRD) levels ≥10−3 at week 12 were assigned to the salvage arm. Maintenance therapy comprised the cyclic administration of 9 drugs during the early treatment phase, followed by the administration of 5 or 6 drugs during the late phase starting from week 14 (SR), 30 (HR/HHR), or 40 (salvage) and lasting until week 156. For central nervous system (CNS) prophylaxis, SR patients received extended triple intrathecal (TIT) injections, beginning on day 1 and repeated every 6 weeks during the first year, every 8 weeks during the second year, and every 12 weeks during the third year. The HR and HHR patients received 18 Gy of cranial radiotherapy (CRT) plus six doses of TIT injections until week 22 of therapy.