ELSEVIER

Blood 142 (2023) 3012–3014

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

622.LYMPHOMAS: TRANSLATIONAL-NON-GENETIC

Outcome of Newly Diagnosed Children and Adolescents with Localized Lymphoblastic Lymphoma Treated on JPLSG-LLB-NHL03 Trial: A Report from the Japan Children's Cancer Group

Masahiro Sekimizu, MDPhD[1], Tomoyuki Watanabe[2], Tetsuya Mori, MD PhD[3], Ryoji Kobayashi, MD[4], Atsuko Nakazawa[5], Akiko M Saito, MD PhD[6], Tetsuya Takimoto[7], Masahito Tsurusawa, MD[8], Keizo Horibe, MDPhD[9], Yasuhiro Okamoto, MD PhD[10], Shosuke Sunami, MD PhD[11]

[1] NHO Nagoya Medical Center, Nagoya, Japan
[2] Aichi Gakuin University, Nisshin, JPN
[3] Department of Pediatrics, St. Marianna University School of Medicine, Kanagawa, JPN
[4] Sappro Hokuyu Hospital, Sapporo, JPN
[5] Saitama Children's Medical Center, Saitama, JPN
[6] Clinical Research Center, NHO Nagoya Medical Center, Nagoya, JPN
[7] National Center for Child Health and Development, Tokyo, Japan
[8] Aichi Medical University, Nagakute, JPN
[9] NHO Nagoya Medical Center, Nagoya, JPN
[10] Kagoshima University, Kagoshima, JPN
[11] Japanese Red Cross Narita Hospital, Narita, JPN

Background: Localized lymphoblastic lymphoma (LL) is rare in pediatric patients and have a favorable outcome. Although the Berlin-Frankfurt-Münster (BFM) 90/95 protocol has been considered standard therapy, this regimen is too intense for patients with localized disease and the total doses of anthracycline and alkylating agents are high. To resolve these problems, we planned a clinical trial to examine the efficacy and safety of a modified BFM regimen for patients with localized LL. We report the 3-year event-free survival (EFS) and overall survival (OS) rate for children and adolescents with localized LL treated on JPLSG-LLB-NHL03 trial.

Procedure: From November 2004 to October 2019, 41 newly diagnosed patients up to 18 years of age enrolled on LLB-NHL03 with localized LL (Murphy stages I and II) and with either T- or B- cell immunophenotype. Staging procedures included: bilateral bone marrow aspirates and biopsies, lumbar puncture, CT or MRI of abdomen, chest X-ray, and bone scintigraphy or whole body bone X-ray. Central pathology review consisted of examination of morphology and immunophenotypic and any available genetic data from the original diagnostic biopsy to confirm the submission diagnosis and assign phenotypic lineage. Treatment consisted of 5 phases: induction (prednisolone 60mg/m ^{2}, day 0-27; vincristine 1.5mg/m ^{2}, day0,7,14,21; cyclophosphamide 1g/m ^{2}, day 0; daunorubicin 30mg/m ^{2}, day 0,7; E.coli L-asparaginase 6,000 units/m ^{2}, 9 total doses, and intrathecal methotrexate and hydrocortisone, day 0,14), consolidation (mercaptopurine 60mg/m ^{2}, day 0-27; cyclophosphamide 500mg/m ^{2}, day0,14; cytarabine 75mg/m ^{2}, 12 total doses and intrathecal therapy methotrexate and hydrocortisone, day 0,14) , CNS prophylaxis (high dose methotrexate 3g/m ^{2}, day0,7,14; and intrathecal methotrexate and hydrocortison, day 0. Standard leucovorin dosing, 15mg/m ^{2} intravenous every 6h, is delivered 36h after the start of the methotrexate infusion and is continued until methotrexate levels are less than 0.1 μmol/L.), delayed intensification (prednisolone 60mg/m2, day 0-13; vincristine 1.5mg/m ^{2}, day 0,7,14; cyclophosphamide 1g/m ^{2}, day0; daunorubicin 30mg/m ^{2}, day 0,7; L-asparaginase 6,000 units/m ^{2}, 6 total doses and intrathecal methotrexate and hydrocortison, day 0,14), and maintenance (mercaptopurine 60mg/m ^{2} daily and methotrexate 20mg/m ^{2} weekly). Total duration of therapy was 24 months from diagnosis. Patients received 120mg/m ^{2} of anthracycline (daunorubicin) , 3 g/m ^{2} of cyclophosphamide and 7 doses of intrathecal therapy.

Results: Of the 41 patients enrolled in the study, 35 were included in the primary efficacy and safety analysis, excluding 6 patients because they did not meet the eligibility criteria: three with diffuse large B-cell lymphoma, one with extranodal NK/T lymphoma, one with mixed phenotype LL, and one with stage III disease. Themedian [range] age at enrollment was 9.0 [2.1-16.1] years. Twenty-three (65.7%) were male. Twenty-nine had pre-B and 6 had pre-T immunophenotype. Fifteen (42.9%) were Stage I and 20 (57.1%) were Stage II. Thirty-four (97%) patients achieved complete remission at the end of induction. The median follow-up for EFS was 10.1 [0.0-15.2] years, and the primary endpoint of 3-year EFS rate [95% confidence interval:

95% CI] (n=35) was 97.1% [81.4-99.6%]. **(Fig.1)** The median follow-up for OS was 10.6 [2.9-16.1] years, and the 3-year OS rate (n=35) was 100%. One pre-T immunophenotype patient with stage II disease failed to achieve complete remission after induction therapy. Overall, patients tolerated therapy well and no treatment-related deaths were observed. There was only one unanticipated adverse event (retinal detachment), and a causal relationship to study treatment was ruled out.
Conclusion: This is the largest trial ever conducted in the treatment of pediatric patients with newly diagnosed localized lymphoblastic lymphoma using an individual protocol. Outcomes of pediatric patients with localized LL treated with 2 years of less-intensive BFM-like therapy was excellent. The number of children diagnosed with localized LL limits the possibility of randomized trials focusing on therapeutic questions. Future studies should identify the biologic or clinical difference between LL and lymphoblastic leukemia, explore less intensive treatment for patients with localized disease, and explore novel targeted therapies.

Disclosures Sekimizu: *Takeda Pharmaceuticals:* Speakers Bureau; *Amgen:* Speakers Bureau; *Kyowa Kirin:* Speakers Bureau; *Ohara Pharmaceutical Co.,Ltd.:* Consultancy. **Horibe:** *Kyowa Kirin:* Consultancy; *Amgen:* Consultancy, Speakers Bureau; *NIPPON SHINYAKU:* Consultancy; *Pfizer Japan:* Consultancy; *Astellas Pharma:* Speakers Bureau; *Chugai Pharmaceutical:* Speakers Bureau; *Novartis Pharma:* Speakers Bureau.

https://doi.org/10.1182/blood-2023-178421

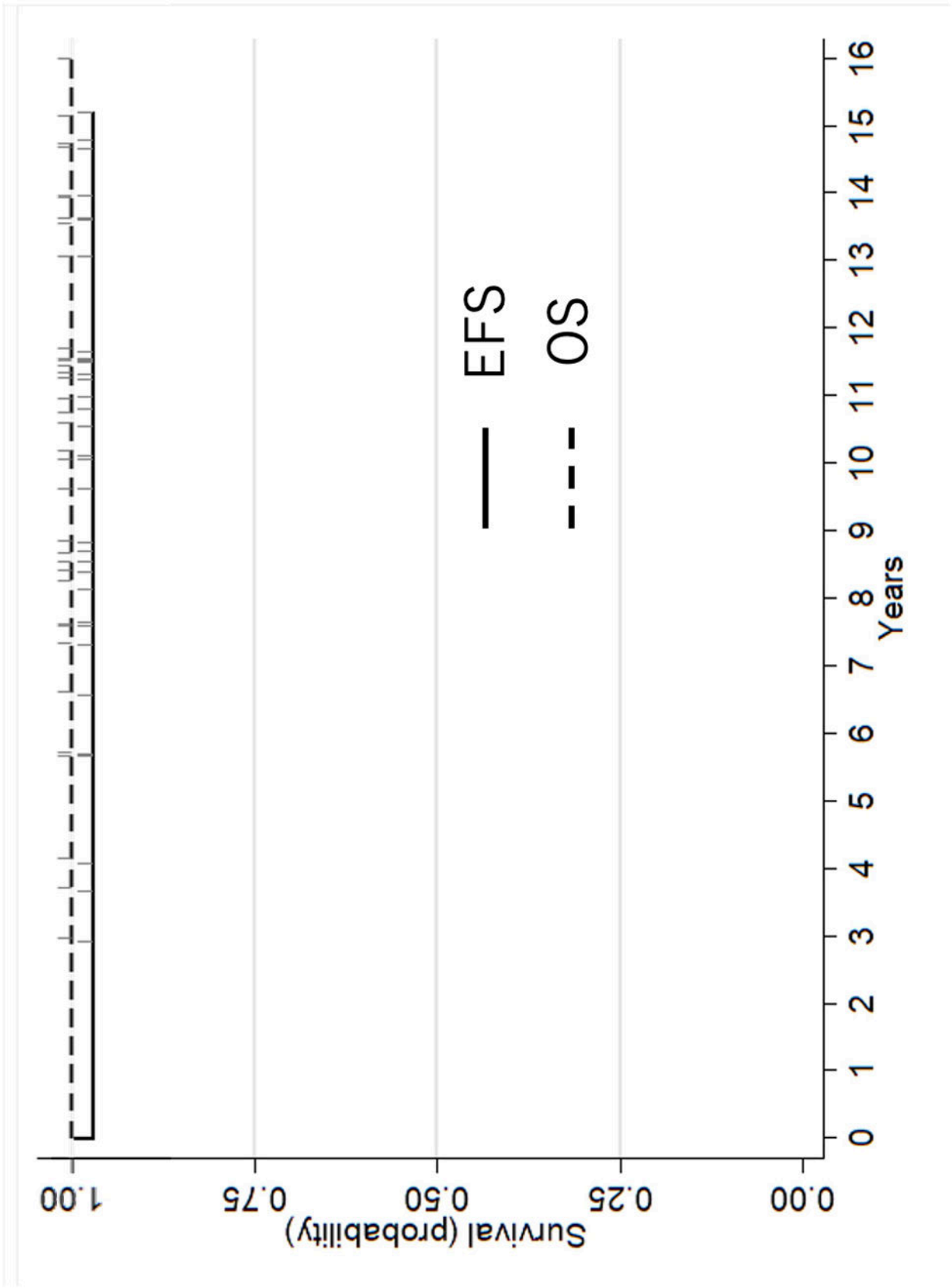

Figure 1