Abstract: P397

Title: AUGMENTED USE OF L-ASPARAGINASE MARKEDLY IMPROVES THE TREATMENT RESULT OF AYA ALL PATIENTS: RESULT OF PROSPECTIVE MRD 2014 STUDY CONDUCTED BY FUKUOKA BLOOD AND MARROW TRANSPLANTATION GROUP (FBMTG)

Abstract Type: Poster Presentation

Topic: Acute lymphoblastic leukemia - Clinical

Background:

The treatment outcomes for adult ALL indicate the need for improvement, leading to the adoption of pediatric ALL regimens for AYA ALL patients.

Aims:

The enhanced utilization of native L-Asparaginase (L-Asp) aims to improve the treatment outcomes for adult non-Ph ALL patients.

Methods:

Patient Eligibility Criteria

Adult ALL patients were enrolled between January 2014 and December 2019 met eligibility criteria, including non-L3 ALL, 16–65 years of age, ECOG performance status of 0–2, and adequate liver and kidney function.

Treatment

Comprised 6 courses of chemotherapy administered in the order of A-B-C-A-B-C regimens, followed by a maintenance. Induction chemotherapy (course A) consisted of CPM; 1000 mg/m2 on day 1, DNR; 50 mg/m2 on days 1, 2, and 3, VCR;1.3 mg/m2 on days 1, 8, 15, and 22, L-Asp; 6000 U/m2 on days 9, 11, 13, 16, 18, and 20, and PSL; 60 mg/m2). The first consolidation therapy (course B) consisted of MIT; 10 mg/m2 on days 2 and 3, AraC; 2000 mg/m2/day on days 1, 2, 3, and 4, L-Asp (10000 U/m2 on day 5) and IT MTX on day 1. The second consolidation therapy (course C) consisted of VCR (1.3 mg/m2 on days 1, and 15), MTX (1500 mg/m2 on days 1, and 15), L-Asp (6000 U/m2 on days 2, and 16) and IT MTX on days 1, and 15. The following maintenance chemotherapy regimen: PSL, 60 mg/m2 on days 1–5; VCR, 1.3 mg/m2 on day 1; L-Asp 10000 U/m2 on day 1; oral MTX, 20 mg/m2 weekly; and oral 6-MP, 60 mg/m2 daily every 4 weeks for ten cycles. Another ten cycles of oral MTX/6-MP every 4 weeks. (UMIN Clinical Trials Registry 000012382)

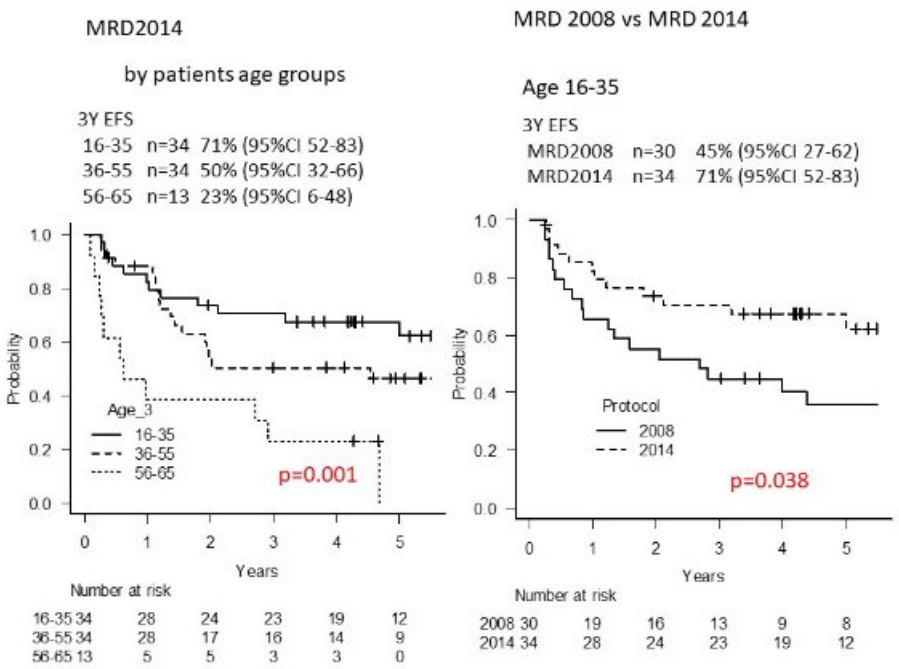
Results:

The median follow-up time was 1128 days (range, 35–2400 days). A total of 81 non-Ph ALL patients (40 males and 41 females; median age 39 years, range 16 to 64 years) in whom MRD status was assessed were included. Among them, 66 cases were classified as B-ALL, 13 as T-ALL, and 2 as MPAL. The median white blood cell count at presentation was 9.9 × 109/L (range 1.0–925.3). There were 6 case of CNS involvement at initial CSF examinations. CR was achieved in 72 patients (89%). The probability of 3-year OS and EFS were 72% (95%CI 61-81) and 55% (95%CI 43-65), respectively. 3-year EFS was 68% (95%CI 50-80) in end of induction (EOI) MRD-negative patients (n = 38) and 36% (95%CI 19-53) in MRD-positive patients (n = 29) (p = 0.012). Analyzing the survival rates by patient age groups (16-35, 35-55, 55-56), the probability of 3-year OS and EFS were 85% (95%CI 68-94) vs 69% (95%CI 50-82) vs 46% (95%CI 20-70) p<0.001, 71% (95%CI 52-83) vs 50% (95%CI 32-66) vs 23% (95%CI 6-48) p<0.001, respectively.

Summary/Conclusion:

In this MRD 2014 study, we have modified our protocol to include an augmented dose of native E. coli L-Asp.

Notably, compared to MRD 2008 (UMIN000001519), the total dose of L-Asp has been raised from 36000 U/m2 to 232000 U/m2 in patients aged 16-35, and from 36000 U/m2 to 132000 U/m2 in patients aged 36-65. With this modification, the treatment outcomes for patients aged 16-35 demonstrated remarkable improvement. Specifically, the 3-year OS of MRD 2008 at 63% (95%CI 44-78) significantly increased to 87% (95%CI 71-94) for MRD 2014 (p=0.003). Additionally, EFS showed significant improvement, as depicted in the figure. Thus, our study unequivocally demonstrated the beneficial effects of the augmented use of L-Asp in this AYA population. Conversely, no significant improvement in survivals was observed in patients aged 36-65. The predominant cause of treatment failure in this group was relapse. Consequently, for these "old" ALL patients, innovative approaches, including the use of novel agents such as blinatumomab and inotuzumab ozogamicin, should be investigated.



Keywords: Asparaginase, Measurable residual disease, Adolescents, Acute lymphoblastic leukemia