Table 1. Characteristics of the patients.

Pt.	Sex/age	Hb g/L	WBC×10⁶/L	%BC	PLT×10⁶/L	FAB	Karyotype	CBFβ/MYH11 transcript	Therapy	DFS (months)	OS (months)
1	F/25	9.6	35.9	85	57	M4+E	46,XX,inv(16)(p12q22)(30)	E	ICE FLAN FLAN ABMT	28	29
2	F/62	7.3	22.4	42	11	M4+E	46,XX,inv(16)(p12q22)(12) 48,XX,+8,inv(16)(p12q22), +21(8)	D	ICE FLAN FLAN	39	40

D and E transcripts may be rather similar to that of patients with type A.

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Intensified induction followed by high-dose therapy with autologous peripheral blood stem cell support in poor-prognosis aggressive non-Hodgkin's lymphoma: results of a pilot study

We conducted intensified induction followed by high-dose therapy (HDT) in patients with previously untreated poor prognosis non-Hodgkin's lymphoma (n= 28). The 3-year overall survival and disease-free survival (DFS) rates were 56% and 66%, respectively. The 3-year DFS rate of patients who actually received HDT was 83%.

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It is still unclear whether high-dose chemotherapy (HDT) is beneficial to patients with poor-prognosis non-Hodgkin's lymphoma (NHL). Several randomized trials regarding this topic have yielded conflicting results.[1-6] It is notable that the trials which suggested a possible benefit of HDT included full-course conventional-dose induction[1,2] or intensified induction,[3,4] whereas the other trials which did not find a superiority of HDT contained abbreviated-course conventional-dose induction.[5,6] These results would suggest that, to be beneficial, HDT should be done as consolidation when the tumor burden after induction is minimal. On this hypothesis, intensified induction might be more reasonable than full-course conventional-dose induction because an intensified induction could induce more patients to

Table 1. Pre-treatment characteristics of the patients.

	n = 28
Sex	
Male	17
Female	11
Age	
Median	46
Range	15-60
Histology (Working Formulation)	
Diffuse large cell	19
Diffuse mixed	4
Lymphoblastic	3
Large cell immunoblastic	2
Histology (REAL classification)	
Diffuse large B-cell	17
Anaplastic large cell	4
Peripheral T-cell, unspecified	3
Precursor T-lymphoblastic	2
Precursor B-lymphoblastic	1
Angioimmnunoblastic T-cell	1
Performance status	
0, 1	19
2	9
Stage	
II	1
III	10
IV	17
LDH	
≤ Normal	2
> Normal	26
Extranodal involvement	
0, 1 site	16
≥ 2 site	12
Bone marrow involvement	
Yes	8
No	20
Bulky disease	
Yes	11
No	17
B-symptoms	
Yes	8
No	20
Aa-IPI score	
2	23
3	5

Aa-IPI: Age-adjusted International Prognostic Index.

achieve the status of minimal residual disease before potentially curative HDT.

We performed highly intensified induction with the regimen described by the Vanderbilt group[7] in patients aged 60 years or less with previously untreated aggressive NHL having 2 to 3 adverse prognostic factors according to the age-adjusted International Prognostic Index.[8] Induction consisted of two intensive courses (C1 and C2) delivered 4 weeks apart. Peripheral blood stem cells (PBSC) were collected under G- or GM-CSF stimulation after C2. Patients who achieved more than a partial response (PR) to induction were to receive high-dose BEAM therapy[9] with PBSC support. Patients who achieved more than a PR but could not receive HDT were to receive 4 cycles of CHOP. HDT was to be performed within 8 weeks from the start of C2.

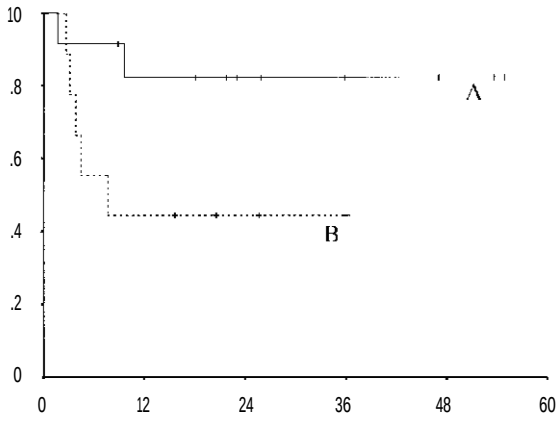

Figure 1. Disease-free survival (DFS) curves of patients with complete response (CR). A: DFS of patients with CR who received high-dose therapy (HDT). B: DFS of patients with CR who did not receive HDT.

Twenty-eight patients were enrolled into the study. The pre-treatment clinical characteristics of the patients are listed in Table 1. After induction, 23 patients achieved more than a PR, 19 a complete response (CR) and 4 a PR. Four patients had progressive disease and one patient died of septic shock during induction. Of these 23 potential candidates, 10 patients did not undergo HDT. Seven patients refused HDT due to poor tolerance of induction and 6 out of these 7 patients were aged over 50 years old. In general, patients over the age of 50 years presented more severe asthenia than patients under the age of 50 years during induction. One patient refused HDT due to financial problems. Two patients could not receive HDT due to inadequate numbers of CD34 cells collected (0.5 and 1.3×10^6 CD34 cells/kg). Two out of the 4 PRs were converted to CR with subsequent therapy: one after CHOP and the other after HDT. Overall, the CR rate after the completion of treatment was 75%. The median follow-up duration of surviving patients was 33 (11 to 57) months. Sixteen patients are currently alive with 14 in continuous first CR. The 3-year overall survival (OS) rate of all patients was 56%. The 3-year disease-free survival (DFS) rate of patients with CR was 66%. In univariate analysis for DFS, there was no factor significantly affecting DFS. A trend towards a higher DFS was observed in patients with CR who actually received HDT compared to in patients with CR who did not receive HDT (3-year DFS rate 83 vs. 44%, $p = 0.06$) (Figure 1). Although febrile neutropenia occurred in almost all patients during the induction and HDT phases, most infections were not fatal except for in 2 patients over the age of 50 years: one 55-year old died of septic shock during induction and another 54-year old died of cytomegalovirus pneumonia following HDT.

Our study shows that highly intensified induction followed by HDT with PBSC support is feasible in patients younger than 50 years, and suggests that patients with aggressive NHL of poor-prognosis are likely to achieve long-term DFS with HDT if they get a good response to induction prior to HDT, at least those who are less than 50 years old. Considering the fact that most potential candidates under the age of 50 years received HDT and most potential candidates over the age of 50 years did not receive HDT, the different DFS between the HDT group and the non-HDT group could also have been affected by the biological heterogeneity of NHL in different age groups. It is difficult to make a definitive assessment of the impact of our therapeutic approach on survival of poor prognosis NHL considering the lim-

itations of our study that enrolled only a small number of patients. To test the hypothesized benefits of our approach, considering its feasibility, it should be studied in a larger cohort of patients under the age of 50 years.

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Performance evaluation of the CoaguChek S system

This evaluation was performed to investigate the agreement of international normalized ratio (INR) test results obtained with the new CoaguChek S system and the current CoaguChek system. The bias between the systems was negligible. The regression lines were not significantly different from the line of identity. The CoaguChek S meters showed a significantly lower meter-to-meter variability than the CoaguChek meters.

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The CoaguChek system is a portable device designed for measuring the prothrombin time (PT) in point-of-care testing and in patient self-testing. The international normalized ratio (INR) scale of the system has been calibrated by the manufacturer (Roche Diagnostics, Mannheim, Germany) in accordance with WHO recommendations.[1] The CoaguChek PT test gives reliable results[2] and has proved its worth in over 50,000 patients performing self-management of oral anticoagulation.[3]

The new CoaguChek S system was introduced recently, with improvements in size, design and user-friendliness. It uses the same test strips as the CoaguChek system. The aim of the performance evaluation study presented here was to investigate the agreement of the INR results obtained with the CoaguChek S and the CoaguChek systems.

A venous whole blood sample from each of 38 patients was analyzed in parallel on 24 CoaguChek meters and 24 CoaguChek S meters using two different lots of test strips (lot 152 and 153). Quality control measurements with CoaguChek PT control solutions were carried out each test day on all meters. In addition, the corresponding citrated plasma of each patient was collected, stored frozen, and tested using three different thromboplastins: Neoplastin, Hepato Quick (Roche Diagnostics, Mannheim, Germany; STA Compact analyzer) and Innovin (Dade-Behring, Marburg, Germany; MLA 900 analyzer). The statistical methods used to evaluate the results were: a) bias including 95% confidence interval (CI) in Bland-Altman-plots;[4] b9 regression analysis by the method of Passing and Bablok;[5] c) relative bias: mean of all [(INRCCS – INRCC) / INRCC]; d) analysis of variance; e) Bennett's test for the comparison of coefficients of variation (CV).

Results. All determinations with liquid quality control solution were found to be within the specified control range. For each patient, a series of 12 measurements was performed for each of the two test strip lots on each of the two types of meter. The coefficients of variation (CV) for the measurements, calculated from the individual values of all 38 patients, ranged from 5.2 to 6.7%. The CV of the meter-to-meter variability for the 24 CoaguChek S meters was 1.1%, compared with 3% for the 24 CoaguChek meters ($p<0.01$). In the case of CoaguChek S, individual meters showed fluctuations in data varying by between -1.9% and +2.0% of the overall mean value.

Comparisons between the CoaguChek S and CoaguChek systems. Regression analysis of the measured data yielded a correlation coefficient of > 0.99. The slopes of the regression lines for the combined and the individual lots were not significantly different from 1. The bias in the data obtained with CoaguChek S and CoaguChek was –0.03 INR (CI: -0.004 to –0.049), corresponding to a relative bias of -0.9%. This bias was statistically