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The Results of High Risk Acute Lymphoblastic Leukemia and Non-Hodgkin's Lymphoma Total Therapy *

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A. Introduction

The study was designed to evaluate the efficacy of seven-drug systemic therapy and three-drug intrathecal treatment in children with high risk acute lymphoblastic leukemia (ALL) and non-Hodgkin's lymphoma (NHL). The modified LSA_2L_2 treatment protocol applied for this study is presented in Fig. 1. The total duration of the treatment was 2.5 years. Estimated distribution of continuous remission and survival were calculated using the product limit method of Kaplan and Meier [3]. The differences in remission and survival were compared according to the nonparametric long rank test [5].

B. Acute Lymphoblastic Leukemia

A group of 92 previously untreated children, diagnosed with ALL from 6 hematologic centers, were eligible for this study. The prognostic stratification of patients was made by BFM score system [2]. The increased risk (IR) group was defined by score numbers 3–10. Overall survival and

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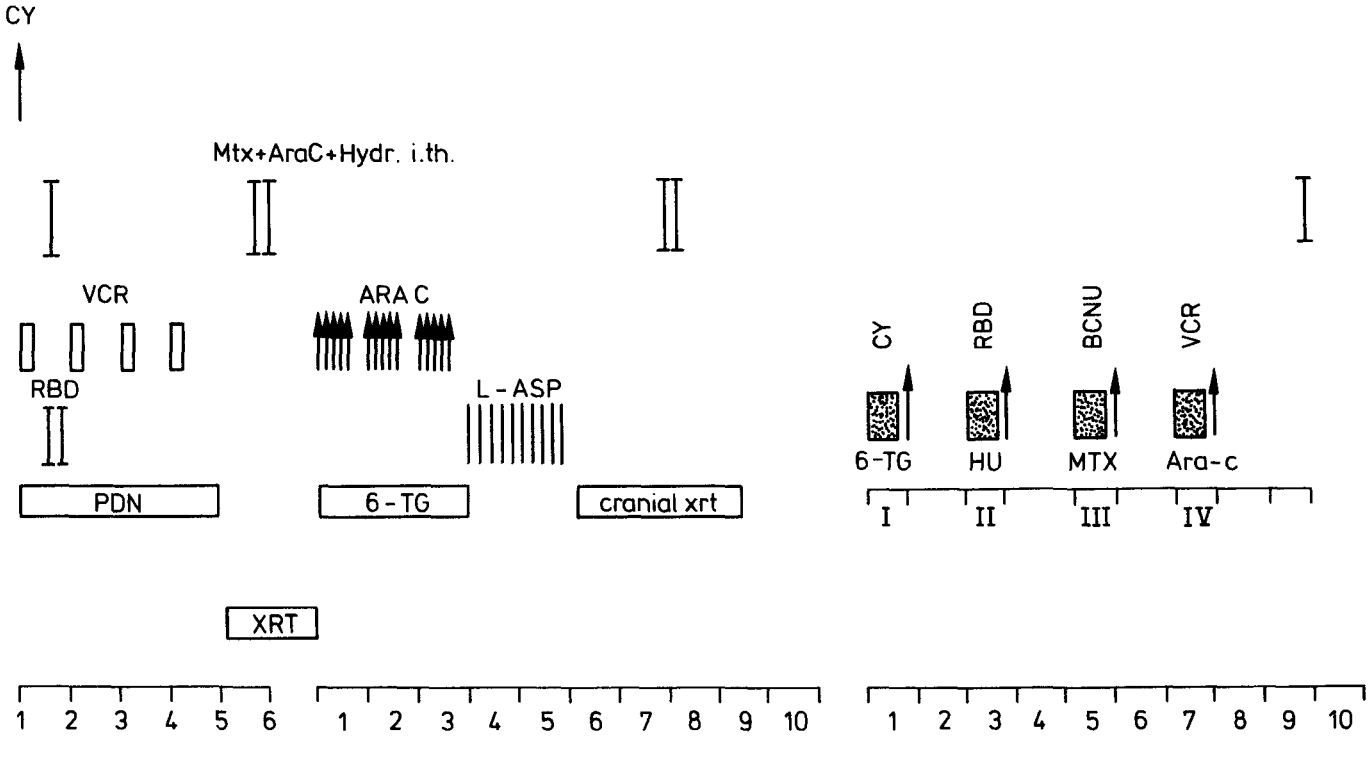
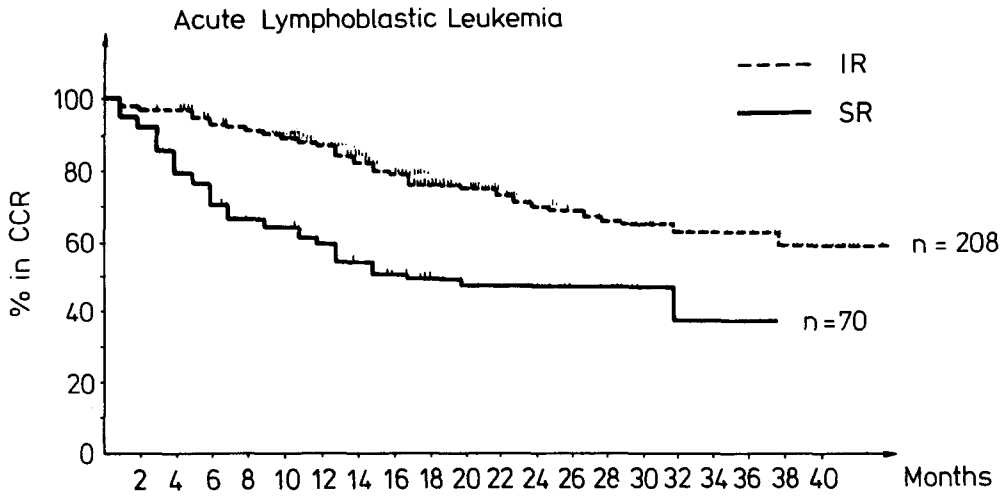
Fig. 1. Modified LSA_2L_2 protocol





	Admitted to study	Achieved complete remission	%	no remission	%	p
SR	212	208	93	4	2	0.01
IR	92	70	76	22	24	
total	304	278	91	26	9	

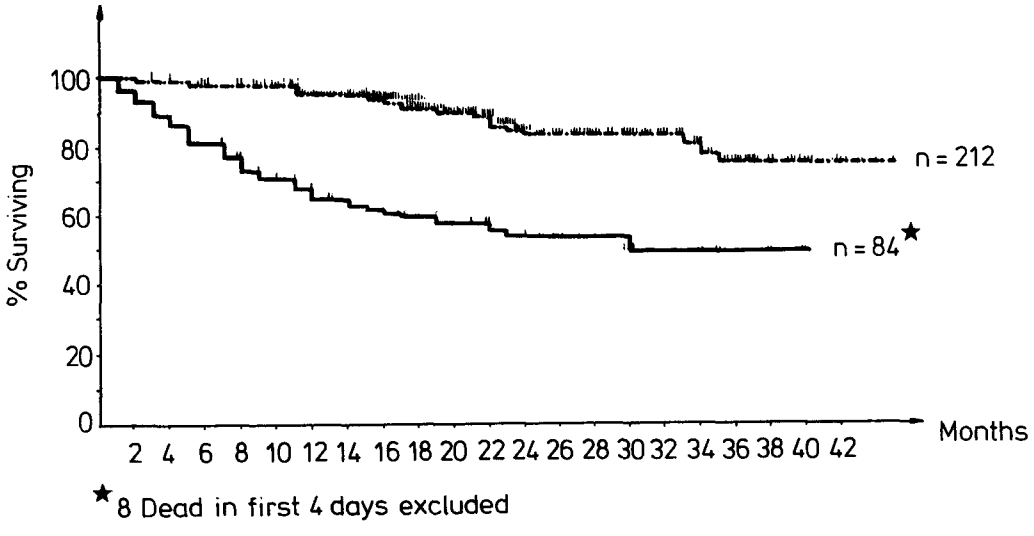


Fig. 2. Remission and survival results

CCR duration of IR and SR patient groups are presented in Fig. 2.

Intensification of the induction, preventive CNS treatment, consolidation and maintenance therapy in the high risk ALL patients has resulted in some increase of disease-free and overall survival duration. However, a considerable proportion of induction failure associated with initial CNS leukemia and high WBC count has been observed. In contradiction to some other studies [6], the frequency of CNS relapses remained relatively high, despite intensification of CNS preventive therapy. The high proportion of fatal infectious complications in the maintenance period suggests their relation with immunosuppression caused by the therapy used, despite the intermittent regimen applied. Our data, like others [7], failed to show evident advantage of the modified LSA_2L_2 protocol for the ALL children with score numbers 6–10.

C. Non-Hodgkin's Lymphoma

A total of 97 previously untreated children with NHL were admitted to this study. Staging was done according to the criteria proposed by Murphy [4]. Histologic diagnoses were made according to the Kiel classification. The most common location of tumor was mediastinal mass followed

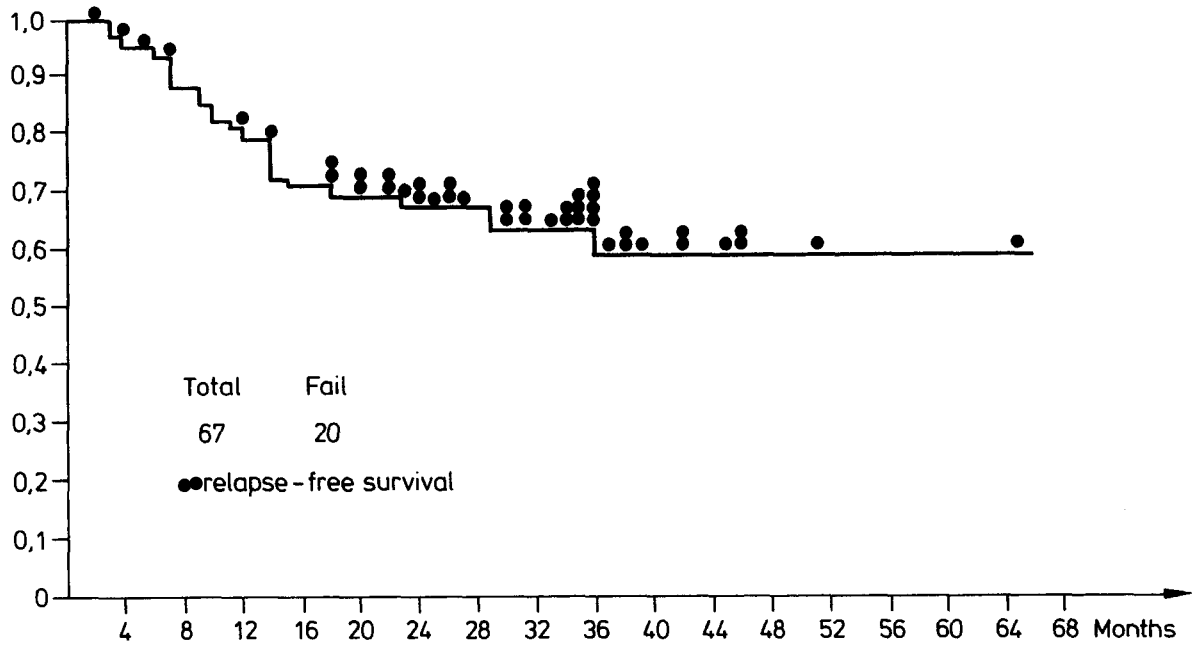


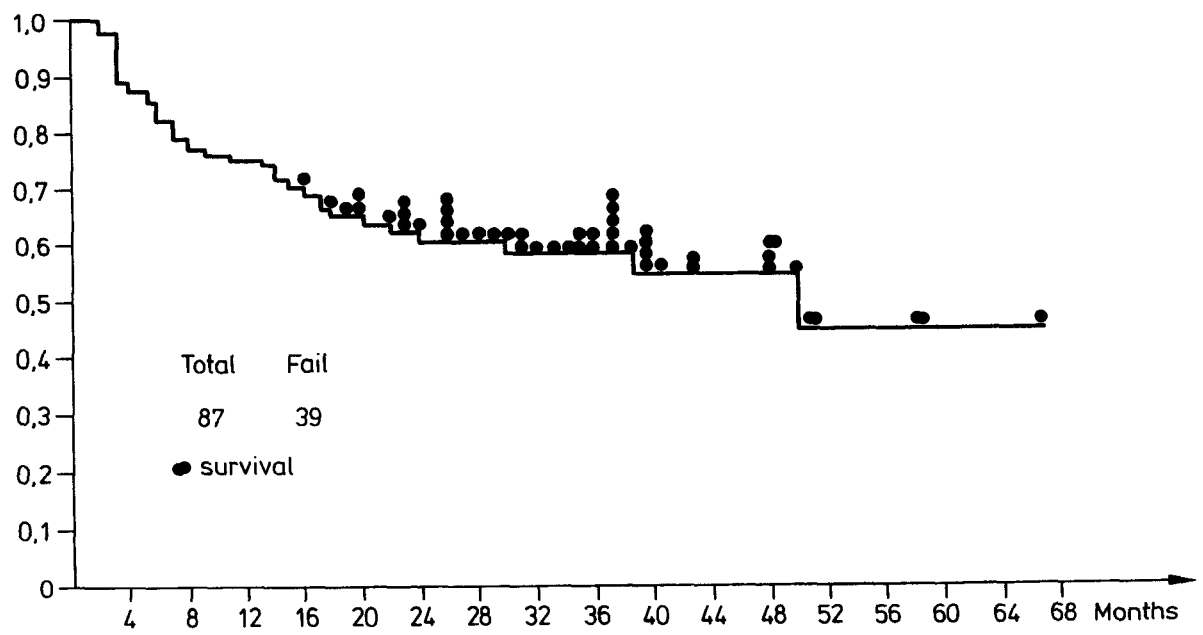
Fig. 3. Relapse-free survival of patients who attained complete remission with LSA_2L_2 treatment

next in frequency by head–neck and abdominal. A total of 22 children received 5 intrathecal doses of methotrexate, cytosine arabinoside, and hydrocortisone, and cranial irradiation, starting at the end of the consolidation phase. After completion of the induction period, radiotherapy (1400–3500 rad) was given to 59 children.

Fig. 4. Overall survival of patients treated by the LSA_2L_2 regimen

The overall estimate of survival and CCR duration and their relation to histologic type of NHL for complete responders are shown in Figs. 3–5. Of the 67 complete responders, 6 had relapses in the bone marrow, 7 in the CNS, and 7 localized relapses. In only 1 of 22 children with CNS prophylaxis was CNS relapse observed, in comparison with 7 of 39 who were not given cranial irradiation combined with cytostatics.

The overall results of NHL study represent a significant improvement over our historical controls [1]. However, there were evident differences in outcome between lymphoblastic and nonlymphoblastic NHL. These data suggest that the histologic type



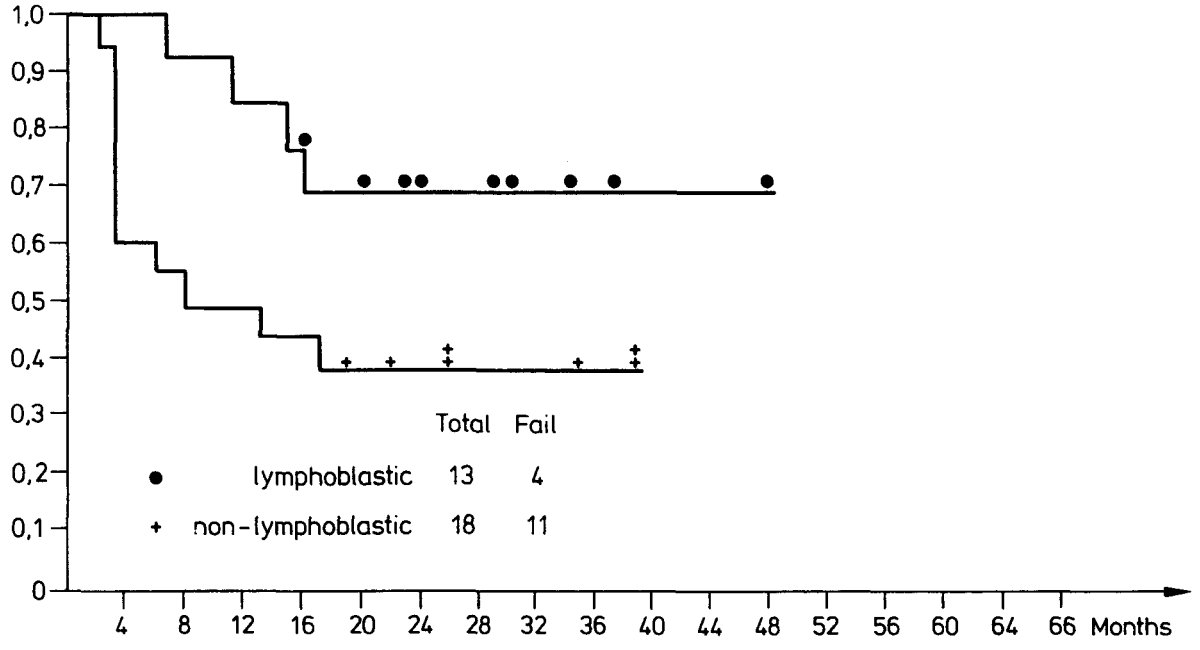


Fig. 5. Survival of patients with nonlocalized disease treated by the LSA_2L_2 regimen according to histologic subtype

of NHL must be taken into account in planning the therapy, and that the LSA_2L_2 protocol is not efficient for non-lymphoblastic subtypes of NHL.

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