*Malignant Lymphomas*

## Adult acute lymphoblastic leukemia, Burkitt`s lymphoma and lymphoblastic lymphoma in middle Norway 1985-2004

**We report a population-based investigation on adult acute precursor B lymphoblastic leukemia, Burkitt`s lymphoma and T lymphoblastic lymphoma in a defined geographic area. The age-adjusted incidence rates for the three diagnostic groups were 0.47, 0.16 and 0.2 per 100000 per year, respectively. Clinical characteristics and outcome following treatment are reported.**

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There are few reports on the incidence and outcome of lymphoblastic lymphoma and leukemia and Burkitt`s lymphoma in unselected patients in defined geographic areas. For T lymphoblastic lymphoma and leukemia we have not found any clearly defined population-based study reporting incidence rate. According to a Dutch register, the incidence rate for Burkitt`s lymphoma is about 0.2 per 100000 per year for adult individuals in the age range from 16 to 60 years, and increases with age over 60 years.[1] For adult acute lymphoblastic leukemia, data from the Northern Health Region in England,[2,3] indicate an incidence rate of about 0.6 per 100000 per year for patients above 15 years of age. Due to the scarcity of reports based on population studies we find it appropriate to present incidence data from the health region of middle Norway and give estimates for outcome for all diagnosed patients through a 20-year period.

Seventy-eight patients, 15 years or older, were diagnosed with lymphoblastic leukemia or lymphoma or Burkitt`s lymphoma from 1985 to 2004. All hematology data and biopsy specimens were re-analyzed and the patients retrospectively classified according to the WHO classification system[4] as having precursor B lymphoblastic leukemia (n=44), Burkitt`s lymphoma including Burkitt type acute leukemia (B-ALL) (n=15) and precursor T lymphoblastic lymphoma including T lymphoblastic leukemia (T-ALL) (n=19). Table 1 gives an overview of all patients. The mean population in the health region in the study period was 633000 with 505700 being 15 years and older and 377900 in the age range from 15 to 59 years. The age-adjusted incidence rate for precursor B ALL was 0.47 per 100000 per year, and 0.43 in the age interval from 15 to 59 years (31 patients, median age 28 years). The incidence rate for Burkitt's lymphoma/B-ALL was 0.16 and for T lymphoblastic lymphoma/T-ALL 0.2 per 100,000 per year. In the acute leukemia group, the diagnosis in the first 5 years was based on morphological and cytochemical criteria. Thereafter, phenotypic verification was performed. One patient had lymphoblasts with co-expression of myeloid membrane markers. Two patients among 16 tested cytogenetically showed the 9;22 translocation. In the Burkitt`s lymphoma/leukemia group six patients were histologically classified as having classic Burkitt`s lymphoma and five as as having Burkitt-like lymphoma. Four of the patients were in stage I at diagnosis. Bone marrow involvement was found in four of the 11 lymphoma patients and in four patients presenting with leukemia only. All lymphoma patients tested positive for CD19 or CD20 and negative for TdT. All patients, but one, with T lymphoblastic lymphomas presented with a mediastinal mass; three had clinical signs of venous obstruction. In three patients the mediastinal mass was the only manifestation of the tumor. Bone marrow involvement was found in six lymphoma patients and in five patients presenting with leukemia only. All lymphoma patients were positive for CD3 and CD7 or CD43 and all tested were positive for TdT.

Treatment protocols used for T-lymphoblastic lymphomas/leukemia and for Burkitt's lymphoma patients were changed in 1992 from CHOP-based regimens with or



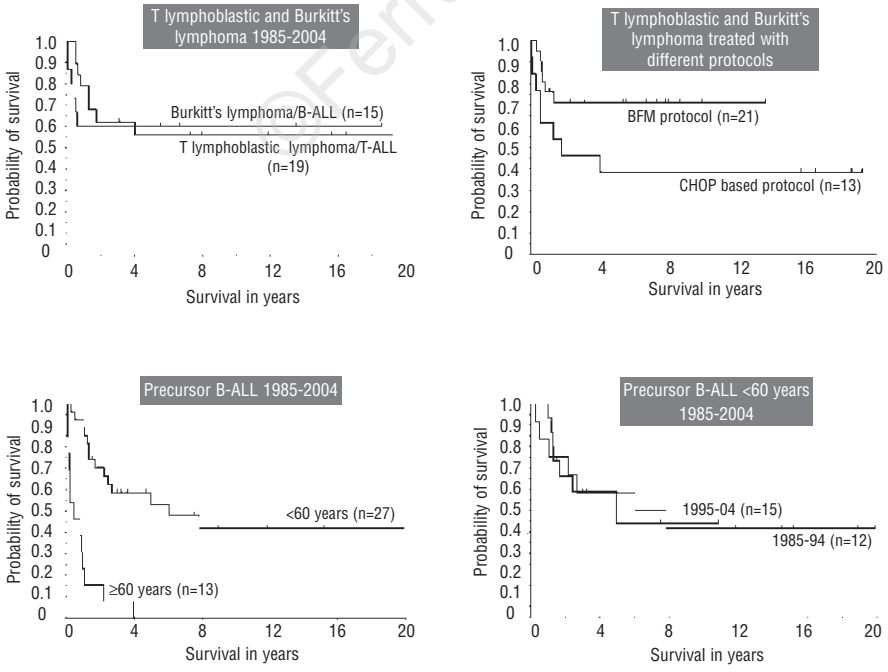


**Figure 1.** Overall survival of patients with T lymphoblastic lymphoma/T-ALL and Burkitt`s lymphoma/B-ALL separately (upper left) and together following treatment with BFM protocols and CHOP-based protocols (upper right). Overall survival of patients with precursor B-ALL above and below 60 years of age (lower left) and separately for the first and second decades of the study period (lower right). Four patients treated with Nordic pediatric protocols (NOPHO) are not included.

**Table 1.** Presenting data and outcome for all patients diagnosed 1985-2004.

| | *Precursor B lymphoblastic leukemia* | *Burkitt/Burkitt's-like lymphoma B-ALL* | *T lymphoblastic lymphoma leukemia* |
|---|---|---|---|
| No. of patients | 44 | 15 | 19 |
| Age, median (range) | 37 (15-84) | 29 (15-70) | 28 (15-65) |
| Gender, male/female | 18/26 | 14/1 | 14/5 |
| Hgb, median (range) | 9.4 (3.9-13.5) | 13.1 (8.7-16.0) | 12.8 (5.8-15.3) |
| Leuk, median (range) | 10.9 (1.4-383) | 8.4 (3.8-22.8) | 8.0 (0.9-227) |
| LDH, median (range) | 1092 (271-7808) | 983 (328-14371) | 790 (273-7220) |
| No in complete remission | 34* | 12* | 14 |
| Subsequent relapse | 18 | 3 | 8 |
| Stem cell transplanted | | | |
| autotransplanted | 0 | 2 | 7° |
| allotransplanted | 9° | 0 | 2 |
| Died within 3 months | | | |
| from complications | 5# | 0 | 0 |
| from lymphoma/leukemia | 2 | 2 | 0 |
| Died later than 3 months | | | |
| from complications | 3# | 0 | 0 |
| from lymphoma/leukemia | 16 | 4 | 8 |
| Disease free survivors | 16§ | 9 | 10§ |
| median observation time, years | 8.9 | 7.7 | 9.9 |

**In the precursor B leukemia group, 30/31 under 60 years of age and 4/13 over 60 years obtained complete remission. In the Burkitt lymphoma/B-ALL group, 9/11 of the lymphomas and 3/4 of B-ALL patients obtained remission. °Three of seven autotransplanted T lymphoblastic lymphomas/leukemia patients subsequently died. Seven of nine allotransplanted precursor B leukemia patients died either from complications or following leukemic relapse; #four of five patients that died from complications within 3 months were over 60 years. One elderly patient died with sudden cardiac arrest. The three later deaths from complications followed stem cell transplantation. §One additional patient is alive with leukemia related disease. All patients were followed-up until 31.12.2005.*

without autologous stem cell transplantation to the BFM protocols 04/89 and 05/93 of the German multicenter study group for adult ALL (GMALL).[5,6] Overall survival for these groups are shown in Figure 1 for the whole 20-year period (log rank test $p$=0.8) and specified for the two regimens ($p$=0.06). No difference was observed regarding remission rates and complications.

Three elderly patients with precursor B-ALL were given palliative treatment. Four adolescent patients were treated according to the Nordic pediatric ALL (NOPHO) protocol. The remaining were treated according to protocols based on information from the Hammersmith Hospital in London with multiple drugs in combination in the induction phase, followed by consolidation drug courses including high dose methotrexate The alterations carried out through the period were mainly in the dose of asparaginase used in induction and in the composition of the consolidation regimens. No difference was observed in survival between the first and second decades of the 20-year period ($p$=1.0) (Figure 1). The proportion of disease-free survivors was about equal for the Burkitt's lymphoma/B-ALL and the T lymphoblastic lymphoma/T-ALL groups (Table 1). The proportion of disease-free survivors in the precursor B ALL group was 0.36. For the patients below 60 years of age the estimated 5 year overall survival was 50% (Figure 1) which compares well with the rates in large international studies.[7] The outcome of patients over 60 years old was similar to that reported in a study from Newcastle[8] in which only two of 19 patients over 60 years old given aggressive treatment survived for more than 2 years in remission.

In conclusion, our data show improved survival for T lymphoblastic lymphoma/leukemia and Burkitt's lymphoma/leukemia after the introduction of the GMALL BFM treatment protocols, while no improvement was noted in the treatment of precurcor B-ALL through the 20-year period. Aggressive cytostatic treatment does not seem to be of real value for patients above 60 years of age.

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*Key words: acute lymphoblastic leukemia, Burkitt`s lymphoma, lymphoblastic lymphoma, population-based investigation, incidence rates.*

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