270  SERUM LEVELS OF SOLUBLE CD30 IN PEDIATRIC ANAPLASTIC LARGE CELL LYMPHOMA (ALCL): A CHILDREN'S ONCOLOGY GROUP REPORT

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Background: The majority of childhood ALCL is characterized by translocations involving the ALK gene. The neoplastic cells of ALCL express in their surface the CD30 antigen, a member of the TNF receptor family that is released into the circulation. Increased levels of soluble CD30 (sCD30) have been found to correlate with disease activity in adults with ALCL however its clinical significance has not been well studied in children.

Methods: Serum samples were obtained at diagnosis, end of induction, end of therapy and at relapse in patients enrolled in ANHL011 protocol for advanced childhood ALCL. Soluble CD30 was measured by an ELISA assay (DAKO). The relationship between sCD30 levels and patient characteristics was examined. Associations between sCD30 and patient characteristics were evaluated using t-tests and ANOVA models. The Kaplan-Meier method was used to estimate event-free (EFS) and overall survival (OS) distributions and the log-rank test was used to compare survival distributions (< median group vs > median group). Cumulative incidence methods were used to look at sCD30 as a predictor of relapse, as death as a competing event. Linear mixed models were used to compare sCD30 levels over time. P-values less than 0.05 are considered to be statistically significant.

Results: Of the 115 eligible patients for analysis, 72 ALK+ patients had sCD30 values at diagnosis and 90 had levels at one or more time points. There were no associations found between patient characteristics and sCD30. Levels of sCD30 were significantly higher at diagnosis and relapse, than those at end of induction and end of therapy (p<0.0001). Sixty four were alive at last contact with a median follow-up of 3.2 years (range: 0.1-5.8 years). sCD30 was predictive of OS with 3-year survival rates in the < median group of 97% (95% CI: 82%-100%) vs. 76% (95% CI: 54%-88%) in the > median group, (median sCD30 is 3468). sCD30 was marginally predictive of EFS (p=0.07), but not of cumulative incidence of relapse.

Conclusions: sCD30 is a valuable marker for disease activity and may have prognostic significance in childhood ALK+ ALCL.

271  ISOLATED MYC REARRANGEMENT BY CYTOGENETICS/FISH IN CHILDREN AND ADOLESCENTS WITH STAGE III/IV B-NHL BM+ AND/OR CNS+ MAY HAVE AN IMPROVED OUTCOMES FOLLOWING IMMUNOCHEMOTHERAPY: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP

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Background: The prognostic relevance of secondary karyotypic abnormalities in C & A with BL has been the subject of several recent studies and had been reported to impact the clinical outcome (Poirel/Cairo et al. Leukemia, 2009, Nelson/Cairol/Sanger et al. BJH, 2010). Methods: Patients with advanced disease were treated with FAB group specific chemotherapy similar to LMB/FAB 86 with the addition of rituximab (Cairo et al. ASCO 2010). Cytogenetic analysis was performed on bone marrow, lymph node, soft tissues, body fluid or bone as previously described (Poirel/Cairo et al. Leukemia, 2009). FISH studies were performed on interphase cells from corresponding samples utilizing a dual-color MYC/FITC translocation probe designed to detect t(8;14)(p11;q32) or a dual-color MYC/breakpoint probe to rearrangements of the MYC gene region at 8q24.1.

Results: Among the 36 patients 15 were FAB group B and 21 group C. Cytogenetic studies were attempted in all 36 cases, but resulted in abnormal findings in only 26 (72%). FISH analysis was successful in 24 of the 36 cases (67%). Ten cases (28%) were either normal or unsuccessful by cytogenetics but were positive for a MYC rearrangement by FISH. Cytogenetically, 25/26 cases exhibited a MYC rearrangement and 11 cases (42%) showed this to be the sole karyotypic abnormality. The most frequent secondary karyotypic abnormality was gain of 1q (8/26, 31%). Other frequent secondary changes included loss of 1q (19%), loss of 6q (19%), gain of 7q (15%), and loss of 17p (12%). The evaluable pathology results were as follows; 29 BL, 1 DBCL and 1 B-cell NOS. The DBCL case was characterized by a t(9;22) and dup(1q), while the B-cell NOS case was characterized by a t(8;14) only. No patients with isolated MYC rearrangement experienced disease recurrence or death. Two patients died of toxic death (1 of Aspergillus, 1 of typhilitis). Two patients with CMYC rearrangement and other cytogenetic abnormalities and one patient with normal cytogenetics died of progressive disease.

Conclusion: FISH analysis is a valuable adjunct study in the identification of MYC rearrangement for diagnosis and risk stratification in advanced C & A-B-NHL. Although preliminary, it appears that in children and adolescents with advanced stage B-NHL and MYC rearrangement as a sole karyotypic abnormality may fare better than those with additional cytogenetic aberrations.

272  A RETROSPECTIVE STUDY TO EVALUATE THE VALUE OF POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY WITH FLUORINE-18-2-D -DEOXY-D-GLUCOSE (PET/CT) FOR THE ASSESSMENT OF REMISSION IN CHILDHOOD NON-HODGKIN'S LYMPHOMA (NHL)

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Background: In adult NHL, large studies have shown that PET Scan is (i) better than conventional imaging for initial staging, (ii) efficient to distinguish residual tumor from fibrous tissues after chemotherapy, and (iii) accurate to predict progression-free survival when performed early after induction chemotherapy.

Methods: We retrospectively reviewed medical and radiological files from children and adolescents with NHL that have been treated in Gustave Roussy Institut and evaluated for remission with conventional imaging and PET/CT.

Results: From 2003 to 2009, 45 children with NHL have been evaluated for remission with PET/CT: 33 Burkitt or large B-cell lymphomas (B-NHL), 6 anaplastic large cell lymphomas (ALCL). 5 lymphoblastic lymphomas (LL) and 1 peripheral T-cell Lymphoma. Medium age at diagnosis was 10.5, 9.1, and 13.4 years for B-NHL, ALCL, LL, respectively. According to St Jude’s classification, there was 3/45 stage I (2%), 9/45 stage II (20%), 23/45 stage III (51%) and 12/45 stage IV (27%) with 9 bone marrow and 2 CNS involvement. For remission’s assessment purpose, sensitivity and specificity of PET/CT compared to histology or follow-up was 33 and 64% for all NHL, with 50 and 57% for B-NHL. PET/CT has a good negative predictive value of 85% for all NHL and 89% for B-NHL. In contrast, the positive predictive value was low with 12.5% for all NHL and 13.3% for B-NHL. Finally, 10/45 patients (22%) also have PET/CT at diagnosis. Among them, initial staging has been modified on PET/CT results.

Conclusion: PET/CT has a good negative predictive value and a low positive predictive value for the assessment of remission in childhood NHL. Further multicentric prospective studies are needed to confirm these results.

273  THE USEFULNESS OF FDG-PET FOR IDENTIFICATION OF BONE MARROW INFILTRATION IN THE STAGING OF CHILDHOOD LYMPHOMAS

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Background: Bone marrow (BM) examination by aspiration and/or trephine biopsy is the standard method for detection of BM involvement in pediatric lymphomas. Iliac crest BM biopsy/aspiration is a painful and invasive procedure, which is affected by sampling errors. Disease outside the iliac crests can be missed. Positron emission
tomography with fluorine-18-fluorodeoxyglucose (FDG-PET) is a non-invasive imaging tool, which offers information on the metabolic activity of tumor cells. PET allows for the evaluation of any area and can detect new lesions at unexpected sites. The aim of our analysis was to evaluate the utility of FDG-PET in detecting BM infiltrates in childhood lymphomas.

Materials and Methods: We retrospectively reviewed 151 staging FDG-PET or PET/CT examination, which were performed in 96 children with newly diagnosed Hodgkin’s lymphoma (HL) and 55 children with non-Hodgkin’s lymphoma (NHL). Twenty-seven patients (18%) had focal BM involvement (clear-cut FDG-avid foci) on PET and were included into this analysis. Patients were aged 4-18 years; 15 had HL, 12 had aggressive NHL (6 B, 5 DLBCL, 1 LL). PET findings were correlated with results of BM examination obtained from an iliac crest aspirates included morphologic and flowcytometry. Eleven children with advanced HL had additional iliac crest BM biopsy. Discordant findings were verified by MRI and follow-up imaging studies including PET.

Results: Of the 27 children with positive FDG PET for BM disease 3 had solitary focus, 24 had multiple FDG-avid lesions. PET detected focal BM disease in pelvis (19 pts), in extremities (18 pts), in spine (15 pts), and in ribs and sternum (6 pts). All these lesions were confirmed by MRI and completely resolved with chemotherapy.

Compared with the results of standard BM examination, concordant positive findings occurred only in 11% of children (3/27). All these children had visible FDG-avid foci in the iliac crest. In other 24 patients PET showed new BM infiltrates, distant from the biopsy site.

Conclusion: In childhood lymphoma FDG-PET is helpful in locating unsuspected lymphoma lesions in the BM. Our analysis showed a surprisingly low sensitivity of microscopic BM examination. Non-targeted BM aspirates/aspirates are not always conclusive because lymphomatous lesions are often located in axill skeleton.

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274 OUTCOME AND PATTERNS OF FAILURE FOLLOWING COMBINED FAB CHEMOTHERAPY AND RITUXIMAB IN CHILDREN AND ADOLESCENTS WITH STAGE III/IV, BM - AND/OR CNS + MATURE B-NHL: A CHILDREN'S ONCOLOGY REPORT

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Introduction/Background: In the previous FAB96 study, variables associated with a significant inferior EFS included advanced stage, elevated LDH, primary mediastinal involvement (PMBL) and combined BM/CNS disease (Cairo et al, ASCO, 2009). Here we report the outcome in those specific high risk sub-categories of advanced childhood mature B-NHL following the incorporation of immunotherapy to the FAB96 chemotherapy backbone.

Patients and Methods: Therapy consisted of FAB B4 or C1 therapy (adriamycin 1 hr infusion) as we have previously described (Patte et al and Cairo et al, Blood, 2007) with the addition of rituximab 375 mg/m2/dose (generously supplied by Genentech) with 2 doses administered in each induction cycle and 1 dose in each consolidation cycle. Eligible patients were evaluated for patterns of failure and toxic deaths after subdividing patients based on risk adapted criteria.

Results: The 3 year EFS (95% CI) for all Group B Stage III/IV and Group C BM/CNS patients were 93% (79-98%) and 89% (73-98%), respectively. Among the 43 evaluable Group B patients there were no toxic deaths, 3 recurrent diseases with 2 disease related deaths. 2/4 patients with centrally reviewed PMBL developed recurrent disease. For non-PMBL histology, 0/19 patients with stage III and LDH < 2X ULN and 1/22 patients with stage III and LDH > 2XULN/ IV developed recurrent disease. No events occurred among 5 patients who received “upstaged” Group C therapy for poor response. Among 40 BM/CNS patients there were 2 toxic and 2 disease related deaths. Of the 26 patients who had isolated Burkitt leukemia there were two toxic deaths and one relapse/death. Among the 14 CNS + patients there was no toxic deaths and 1 recurrent disease/death.

Conclusions: Excluding PMBL histology, with combined modified FAB 96 chemotherapy and rituximab only 5 deaths (2 toxic deaths, 3 disease related deaths) occurred in our cohort of 81 advanced mature B-NHL patients. For patients with PMBL, the high failure rate with group B4 therapy + rituximab, indicates it would be appropriate to investigate new treatment strategies. Alternatively, with the addition of rituximab to the FAB backbone we found excellent tumor control among the remainder of the Stage III/IV (1/41 relapse in non-PMBL), BM+ and CNS+ patients.

275 PRIMARY MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT) LYMPHOMA OF THE THYMUS IN AN ADOLESCENT FEMALE

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Introduction: MALT lymphomas are a distinct clinicopathologic entity included in the 2008 WHO classification of extranodal marginal zone lymphomas.

Materials and Methods: We report the first pediatric case of thymic involvement by this rare lymphoma.

Results: A 14-year-old female, originally from Laos, presented with one week history of painful cervical lymphadenopathy, fever and headaches. She also had chest pain, dyspnea on exertion, pain with swelling, and neck swelling. Blood work showed lymphocytosis, normal renal/liver functions and normal LDH/LI/uric acid.

CT of the chest showed a 6 cm wide left anterior mediastinal mass with cluster of nodes in superior mediastinal and cervical areas. There was no evidence of disease anywhere else.

Bone marrow aspirate and biopsy were negative for malignancy. PET scan showed markedly increased uptake in the mediastinal and perihilar region and both sides of neck. A biopsy showed a cystic thymic mass compatible with extranodal marginal zone – B cell lymphoma (MALT lymphoma) of the thymus stage III. There was no translocation of MALT1 but 3 copies of MALT1 were detected by FISH. Immediate evaluation revealed secondary immune abnormalities with low NK cell count, and high IgA/IgG levels.

Treatment regimen included rituximab, cyclophosphamide, vincristine and prednisone (R-CVP). Evaluation of her response after 3 cycles of CVP revealed a significant reduction in the mediastinal mass with disappearance of cervical nodes on CT, and a markedly reduced FDG uptake on PET scan. A second evaluation after another cycle of R-CVP did not show any further improvement. Therefore, she received 3020 Gy involved field radiation therapy to the mediastial and neck areas. Maintenance therapy with rituximab every six months for two years is currently in progress, and she is in complete remission at eight months from diagnosis.

Literature review suggests that more than 75% of patients with thymic MALToma are Asians, 81% of them have autoimmune disease or hyperglobulinemia and 79% have macroscopic cysts (without any specific histology).

Conclusions: Thymic MALT lymphoma is a rare pediatric lymphoma. Although the follow-up time is short, treatment with rituximab combined with an alkylating agent and local radiotherapy was beneficial.

276 HEMOPHAGOCYTIC LYMPHANGIOTHISCYTOSIS-ASSOCIATED ANAPLASTIC LARGE CELL LYMPHOMA: INCIDENCE, CLINICAL FEATURES AND OUTCOME

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Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a potentially life threatening condition characterized by abnormal activation and proliferation of polyclonal CD8+ T lymphocytes and macrophages that infiltrate multiple organs, including the bone marrow, the lymph nodes, the spleen, the liver, and the brain. HLH can be either primary, with a genetic etiology, or secondary, resulting of an activation of the immune system associated with malignancies, autoimmune diseases or infections. The association between HLH and pediatric anaplastic large cell lymphomas (ALCL) is uncommon, but few reported cases in literature. The aim of this study was to analyse the incidence, the clinical, biological and histological characteristics and the outcome of HLH associated-ALCLs.

Materials and methods: We reviewed medical files and bone marrow smears of all 50 consecutive children treated for ALK+ ALCL in the pediatric department of the Institut Gustave Roussy between 1975 and 2008. The diagnosis of HLH was made according to the guidelines of the Histioctye Society (HLH-2004 classification) in patients fulfilling ≥ 5/8 of the following criteria: 1) fever, 2) splenomegaly, 3) cytopenia, 4) hemophagocytosis in bone marrow, spleen or lymph nodes, 5) hypofibrinogenemia (<1.5 g/L) and/or hypertriglyceridemia (>2,500 mg/dl), 6) hyperferritinemia (>500 mg/dl), 7) low or absent NK-cell activity and, 8) high levels of sIL-2r (>2,400 U/ml). None of these two last items were routinely tested in ALCL patients.

Results: 6/50 ALCL patients (12%) met at least 5 criteria for HLH including fever (6/6), splenomegaly (4/6) cytopenia (5/6), hemophagocytosis (6/6), hypertriglyceridemia (3/4), hyperferritinemia (4/5). The main differences between HLH-associated ALCL and ALCL without HLH was a higher incidence of lung, CNS and bone marrow involvement whereas there were no significant differences between the two groups in term of histological subtypes and outcomes.

Conclusions: HLH is not rare in pediatric ALCL. Despite of elevated incidence of visceral, CNS and bone marrow involvement in such situations, the presence of HLH has no significant impact on the outcome of children treated for ALCL.
The addition of rituximab to Group C FAB therapy appears to be safe and well tolerated. Preliminary results in a small cohort of children and adolescents with CNS+ mature B-NHL/B-L suggest that the addition of rituximab to FAB Group C therapy without concomitant CNS radiation may reduce systemic relapse (93% OS) Large and/or randomized studies are warranted in the future to test this hypothesis in this previously high-risk subgroup.

279 THERAPY OF MATURE B- NHL/ALL WITH CNS INVOLVEMENT IN CHILDREN WITH CHEMOIMMUNOTHERAPY AND INTRAVENTRICULAR INFUSIONS OF RITUXIMAB

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Background: Primary CNS involvement is an independent risk factor for inferior outcome in children with mature B- NHL/ALL, whereas prognosis of CNS relapses is very poor. According to own data the probability of 4-year EFS and OS in children with advanced stages (III/IV) of mature B-NHL/ALL following chemotherapy (CT) with rituximab are 89%±0.04% (protocol BNLN 2004a). We report on outcome of B-NHL/ALL with CNS involvement in children using CT and rituximab.

Objectives: To determine safety, tolerability and effectiveness of intraventricular injections of rituximab in CNS-positive B-NHL/ALL pediatric pts.

Methods: 6 pts with CNS involvement were included, 4 with primary tumor and 2 with CNS relapse. There were 5 boys and 1 girl aged 4-15 (med 9) y. 3 pts (1 DLBCL and 2 Burkitt lymphoma (BL)) had primary intracranial mass, 1 pt with B ALL was CNS disease with no tumor mass, 1 pt with Burkitt lymphoma had leptomeningeal relapse, one of them with orbital involvement. In all pts Ommaya reservoir was placed. Primary pts were treated according to the protocol BNLN 2004a representing slightly modified BMF90 protocol combined with 4 rituximab (MabThera®) i.v. infusions 375mg/m2 given 1 day before the CT cycles and CNS therapy with Mtx, AraC and Dexa combined with rituximab 25mg N4 intraventricular once in 2-3 weeks. Relapsed pts received courses ICE with rituximab i.v. (N-2) and i.ventr. (N 5) with TIT and in one case (with orbital lesions) + liposomal AraC and thiotepa.

Results: All primary pts are alive in CR 2 pts with residual masses after the 5th CT block received autoPBSCT, one with BM and total neuroaxis involvement achieved CR after the 3d block (rituximab i.v. and i.ventr.N3) one is on therapy without tumor mass after the 4th block. One relapsed pt died due to the tumor progression, one is alive 15 mo after completion of therapy. In total 20 i.ventr. injections of rituximab were performed in 6 pts. We didn’t notice any kind of neurotoxicity, local irritation or severe allergic reaction during or after these procedures.

Conclusions: Using of local (i.th. or i.ventr.) of rituximab 25mg combined with intensive systemic immunochemotherapy in pts with primary mature B-NHL/ALL with CNS involvement is safe and possibly contribute to better outcome.

280 RASBURICASE (RAS) IS SAFE AND EFFECTIVE IN THE PREVENTION AND TREATMENT OF ACUTE TUMOR SYNDROME (ATLS) IN CHILDREN AND ADOLESCENCE UNDERGOING REDUCTION THERAPY FOR MATURE B-CELL LYMPHOMA (MBL): A REPORT FROM THE CHILDREN’S ONCOLOGY GROUP

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Introduction: The most common pediatric mature B-NHL is Burkitt lymphoma (BL). Addition of HD-MTX, HD-cytarabine, and CNS irradiation to LMB Group C therapy for children with CNS+ B-NHL/LBL yielded a 77% 5-yr EFS in the LBMB99 trial (Patte et al., Blood, 2001). An international study (FAB/LMB06) used a similar backbone, but replaced cranial radiation with additional HD-MTX and intrathecal therapy, with similar results (75% 4-yr EFS) (Cairo et al., Blood, 2007). However, patients with combined CNS+ and marrow disease fared worse than isolated CNS+ (61% vs. 83% 4-yr EFS, p<0.001). Over half of CNS+ patients who progressed or recurrent did so systemically, without CNS relapse (Cairo, et al., pers. comm.). Rituximab, a chimeric monoclonal antibody against CD20, improved EFS, PFS, and OS when combined with chemotherapy in adult DLBCL (Cleary et al., N Engl J Med, 2002; Freidman et al., J Natl Cancer Inst, 2003). We sought to determine if adding rituximab to FAB Group C chemotherapy in children and adolescents with CNS+ mature B-NHL/BL would be safe and efficacious.

Methods: Children and adolescents (<21 yrs.) with CNS+ B-NHL/LBL received standard FAB Group C therapy (Cairo et al., Blood, 2007). Rituximab was given at 375 mg/m2/dose twice in COPADIM 1 & 2 and once in each CYVE course (Cairo et al., ASCO, 2010). CNS+ was defined as CSF blasts (>1), cranial nerve palsy (CNP), parameningeal extension (PME), or intra-cerebral mass (ICM).

Results: Of 41 eligible Group C patients, 14 (34%) were CNS+. Eight CNS+ patients had CSF blasts (WBC median 35 (range 1-1104) with 4 cases CNPs, 4 PME+ and 1 ICP+). Of the remaining 27 patients (93%) are alive and disease-free with a mean of 41 mo (14-72). In the 6 BM-/CS+ cases, 100% are NED [mean 45 mo (18-66)]. For BM+/CS+ patients, 7/8 (88%) are NED with a mean of 38 mo (14-72). One patient progressed with both BM-/CNS+ and CNS+.

Conclusions: The addition of rituximab to Group C FAB chemotherapy appears to be safe and well tolerated. Preliminary results in a small cohort of children and adolescents with CNS+ mature B-NHL/BL suggest that the addition of rituximab to FAB Group C therapy without concomitant CNS radiation may reduce systemic relapse (93% OS). Large and/or randomized studies are warranted in the future to test this hypothesis in this previously high-risk subgroup.
were 4.5±2, 9.6±4.6, and 8.6±5, respectively. At presentation, 31% of patients (all groups) had an elevated (> 8mg/dl) UA, and 47% received elective doses of Ras in the days prior to the first day of chemotherapy. The incidence of LTLS prior to Ras for IR NL-LDH, IR HI-LDH, and HR, was 0%, 25%, and 17%, respectively. The incidence of CTLS prior to Ras was 0%, 10%, and 11%. Following the administration of Ras, the incidence of new onset LTLS and CTLS for the entire cohort was 6% (4% with hyperuricemia) and 5% (1% with hyperuricemia) respectively. Peak daily UA levels dropped below 8mg/dl within 2 days in 95% of patients with elevated UA. The GFR improved in all groups, with the most benefit seen the IR HI-LDH group (246%±110) and those with elevated initial UA (259%±108). There were no adverse reactions to Ras.

Conclusions: Ras in combination with COP reduction therapy for children and adolescents with newly diagnosed MBL is safe. Although some patients with MBL present with LTLS and CTLS, the administration of Ras led to substantial improvement of pre-existing TLS, and largely prevented new onset TLS.

281 TREATMENT OF CHILDREN’S B-NON HODGKIN’S LYMPHOMA WITH AND WITHOUT MONOCLONAL ANTIBODIES IN CROATIA

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Introduction: B-non-Hodgkin’s lymphomas (B-NHL) are a group of highly aggressive malignant lymphoproliferative diseases that require rapid diagnosis and prompt therapy initiation.

Aim: The aim of the study was to confirm excellent results recorded in the BFM-NHL trial in Croatia, and to identify appropriate measures to prevent the life-threatening events frequently accompanying the early phase of treatment.

Patients and Methods: During the 1990-2010 period, 35 children with B-NHL (19 male and 16 female) aged 2-16 (mean age 9.8) years, were treated according to the NHL-BFM protocol. Therapy consisted of 5-day pretreatment (standard chemotherapy dosage) combined with 2-6 cycles of high-dose chemotherapy; in addition, eleven patients received monoclonal antibodies (Mabtera®) in 2006-2010. Patients were divided into three risk groups.

Results: Complete remission was achieved in all 35 (100%) patients; disease relapse and lethal outcome were recorded in four (11.4%) patients, i.e. three patients on chemotherapy alone and one patient also administered monoclonal antibodies (meningeal relapse 2 months of treatment completion); in 31 (88.5%) patients, the first complete remission has been persisting to the present. Grade III and IV toxicity was mostly observed after the first and second cycle of chemotherapy. The level of toxicity associated with the first cycle of chemotherapy was considerably lower in patients administered monoclonal antibodies. In one patient, secondary tumor disease (AML) developed 4 years of treatment discontinuation.

Conclusion: Although referring to a relatively small number of patients, therapeutic results were very good and consistent with those reported from other European centers. However, many questions remain to be answered. For instance, should monoclonal antibodies be administered in all patients with B-NHL, or in the high risk group only, or during the first chemotherapy cycle only, or in patients with disease relapse only, or as maintenance therapy in patients with B-ALL/NHL?