

**798 LAMIVUDINE PROPHYLAXIS IN A PATIENT WITH ACUTE MYELOGENOUS LEUKEMIA AND CHRONIC HEPATITIS B**

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Chemotherapy treatment in hepatitis B virus (HBV) carriers could cause in a significant percentage of patients viral reactivation and hepatitis B which can even progress to fatal liver failure. Over the last few years the prophylactic administration of lamivudine as a potent antiviral drug has been tested in this type of patients. The cases that have been reported in the literature are relatively few. They refer almost exclusively to lymphomas and other non-hematological malignancies which were treated with chemotherapy of moderate intensity. To the best of our knowledge, this is the second reported case of a patient with acute myelogenous leukemia and chronic hepatitis B to whom lamivudine was prophylactically administered.

A 47-year-old female was admitted to our clinic and diagnosed with acute myelogenous leukemia. Her medical history showed HBsAg positivity for the past seven years. Biochemical blood tests revealed normal function of liver but serological studies detected positive HBsAg, anti-HBc and anti-HBe with negative anti-HBc-IgM, HBeAg, anti-HCV. PCR method revealed an HBV-DNA titer higher than the highest detectable limit of our laboratory, namely  $> 4 \times 10^7$  copies/ml (normal  $< 1 \times 10^3$ ). Lamivudine therapy was initiated at a dose of 100 mg p.o. daily, two days before chemotherapy treatment. Remission induction chemotherapy consisted of cytarabine 100 mg/m<sup>2</sup> i.v. (continuous infusion) days 1-7, idarubicin 10 mg/m<sup>2</sup> days 1-3 and cytarabine 2g/m<sup>2</sup> days 8-9. After complete remission was achieved, the patient was initially treated with cytarabine 200 mg/m<sup>2</sup> i.v. (continuous infusion) days 1-5 and idarubicin 12 mg/m<sup>2</sup> i.v. days 1-2. The second cycle of postremission chemotherapy included cytarabine 2 gr/m<sup>2</sup> /12 hours i.v. days 1-3 and etoposide 100 mg/m<sup>2</sup> i.v. days 4-5. Throughout the three cycles of chemotherapy and the long periods of severe aplasia (25-30 days) there were no clinical and/or laboratory findings of liver dysfunction. A new viral DNA study 2.5 months after the first evaluation showed an impressive decrease of viral load ( $4.7 \times 10^3$  copies/ml).

Conclusively, lamivudine prophylactic administration was proven to be highly efficacious at preventing hepatitis B flare-up during intensive chemotherapy in a HBsAg positive patient with acute myelogenous leukemia.

**799 COGNITIVE DECLINE IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES**

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**BACKGROUND:** Anemia is a common complication in patients with hematologic malignancies and has great influence on QoL.

**AIMS:** To determine cognitive functions in patients with hematologic malignancies and evaluate the use of Complex Reactimeter Drenovac (CRD) versus Folstein Mini-Mental Status Examination (FMMS) to measure cognitive functioning in cancer trials.

**PATIENTS AND METHODS:** A total of 150 pts with hematologic malignancies in various stage of disease were seen for baseline evaluation. For each patient we collected clinical data, laboratory tests and performed tests measuring cognitive functions (CRD and FMMS), ability to perform activities of daily living (ADLs) and quality of life (QOL), repeated them monthly during six months. In the same time control group (50 healthy pts) of the same age, sex, and education were compared.

**RESULTS:** We found cognitive decline in all hematologic pts. Performance on the tests were strongly related to anemia, cancer treatment, and stage of disease. The worst cognitive functions had pts with acute leukemia and multiple myeloma, especially when anemic. Successful treatment of anemia had great influence on cognitive improvement and depended upon achieved hemoglobin level.

**CONCLUSION:** We applied and compared two tests to determine cognitive changes related to hemoglobin level. Results emphasized necessity of early correction of anemia in hematologic patients.

**800 CLINICAL SIGNIFICANCE OF P53 EXPRESSION IN MULTIPLE MYELOMA**

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**Background:** Mutations of p53 are one of the most often acquired genetic changes in malignant tumors. According previous reports, the mutations of p53 are rare events in patients with newly diagnosed MM. However, there are a few literature data about clinical significance of this protein in MM.

The aim of this study was to evaluate clinical significance of p53 expression in MM.

**Patients and methods:** 59 patients with newly diagnosed MM (27 females and 32 males, median age 62 years) were enrolled in the study. The diagnosis of MM was made according to the criteria of Chronic Leukemia-Myeloma Task Force. Clinical staging was done according to the Durie and Salmon classification (4 patients had disease stage I, 15 patients stage II and 39 patients stage III). The histological grade and histological stage (i.e. volume of myeloma infiltration) were determined according to the models proposed by Sailer and Bartl, respectively. We used standard immunohistochemical analysis with p53 antibody on B5-fixed and paraffin-embedded bone marrow specimens to evaluate expression of p53 in myeloma cells. The specimens were considered positive when equal or more than 5% plasma cells showed nuclear positivity.

**Results:** p53 expression was detected in 9 (15.25%) patients. p53 expression did not correlate significantly with clinical stage (I+II vs. III), 2-microglobulin level ( $\leq 6$  mg/L vs.  $>6$ mg/L), histological grade (I vs. II+III), histological stage ( $< 20\%$  vs.  $21-50\%$  vs.  $> 50\%$ ) and the extent of osteolytic lesions ( $\leq 3$  vs.  $> 3$  lesions). Median survival of patients with p53 immunoreactivity in  $\geq 5\%$  plasma cells was 10 months, whilst median survival of patients with p53 immunoreactivity in  $< 5\%$  plasma cells was 35.8 months. However, this difference was not significant ( $p = 0.2$ ).

**Conclusion:** Frequency of p53 expression in our group of newly diagnosed MM was relatively low. p53 expression was not associated with clinical and histological features of more aggressive disease, nor with the short survival.

**801 GLUTATHIONE PEROXIDASE (GPX) ACTIVITY AND GLUTATHIONE (GSH) LEVEL IN PATIENTS WITH RELAPSED MULTIPLE MYELOMA (MM) TREATED WITH ARSENIC TRIOXIDE (ATO)**

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**Background:** Multiple myeloma (MM) remains an incurable B cell malignancy with median survival rates of 4-6 years. Arsenic trioxide (ATO) is a novel therapeutic option in the treatment of MM. This agent has multifaced mode of anticancer action. One of them is induction of apoptosis by inhibition of the GSH cellular redox system. Arsenic suppresses glutathione peroxidase (GPx) which is the major route for detoxification of reactive oxygen species. Elevated glutathione (GSH) level has been associated with the MM chemoresistant phenotype. Reduced GSH level enhances the apoptotic effects of ATO.

**Aim:** The aim of the study was to assess clinical efficacy of ATO and to evaluate activity of GPx and level of GSH in patients with relapsed MM treated with ATO and ascorbic acid (AA).

**Methods:** 7 patients (4 women and 3 men, mean age 59 years) with relapsed MM were treated with 6 cycles of ATO (Vipham, Poland) 0,25mg/kg iv five days in the week in a 2 weeks on/ 2 weeks off schedule. In addition ascorbic acid 1000mg p.o. was given. All patient were in advanced stage of disease III A acc. Durie and Salmon. GPx activity and GSH levels were measured by spectrophotometry (spectrophotometer SP-8-100 Pye Unicam). Normal range for GPx 27,5 - 73,6 U/g Hb and for GSH 25,5 - 50,0mg%. Statistical analysis was made using Wald-Wolfowitz test ( $p < 0.05$ ).

**Results:** 1 patient achieved partial response and 1 patient had stable disease according SWOG criteria. The common drug related adverse events were mild and resolved spontaneously: cytopenia (3 patients), QT prolongation (1 patient), abdominal pain and diarrhoea (1 patient), peripheral neuropathy (1 patient). In all patients reduced GPx activity was observed. Only in 2 out of 7 patients (one with partial response and one with stable disease) reduced GSH levels were observed. Glutathione (GSH) level and glutathione peroxidase (GPX) activity are presented in the table.

Conclusion: Obtained data although based on relatively small group of MM patients suggest that ATO in combination with AA has clinical activity in multiple myeloma and significantly decreases activity of GPx.

	GSH mg%	GPx U/g Hb
Before ATO + AA	36,34	49,91
After 6 cycles of ATO + AA	31,68	24,07
p	NS	0,003

Caption 1: Glutathione (GSH) level and glutathione peroxidase

**802** EXPRESSION OF KILLER INHIBITORY RECEPTORS: CD94 AND CD158B IN NATURAL KILLER CELLS IN MULTIPLE MYELOMA AND NON-HODGKIN'S LYMPHOMA

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Background: Natural killer (NK) cells express MHC class I-specific inhibitory receptors, termed 'killer inhibitory receptors' (KIRs). Upon binding to MHC class I molecules on target cells, these receptors deliver a negative signal that prevents the NK-mediated lysis of target cells. Different MHC class I-specific killer inhibitory receptors (KIRs) are expressed in vivo by NK cells. There are some reports that expression of CD94 is increased in multiple myeloma (MM) patients. The role of KIR in non-Hodgkin's lymphoma (NHL) is not clearly established.

Aim: The aim of this study was to investigate the expression of KIRs (CD94-NKG2-A receptor complex and CD158b) in NK cells of B cell malignancies: MM and NHL patients.

Methods: 32 MM and 19 NHL patients were studied. Clinical data are showed in the table 1. Patients were studied before any chemotherapy. The control group consisted of 10 age-matched normal donors. The presence of CD94 and CD158b was evaluated in NK cells isolated from MM, NHL patients and normal donors.

Peripheral blood mononuclear cells (PBMCs) were obtained by density-gradient centrifugation (Ficoll-Hypaque) of heparinized venous blood. These were then counted microscopically. Three colour immunofluorescence staining was performed. 7 ml of monoclonal antibodies conjugated with FITC and PE in the case of double colour staining or additionally conjugated with Cy-Chrome (three-colour staining) was added to each tube. We used the following monoclonal antibodies specific for: CD14, CD45 (DAKO, Denmark), CD3, CD56, CD94, CD158b and NKG2A (Becton Dickinson, USA). Tubes were than agitated and incubated for 20 min. at 4oC in the dark, after which 5 ml of PBS-Ca2+Mg2+ containing 0,1% NaN3 (Sigma Chemical Co., St Louis, Mo, USA) was added to each tube and pelleted by centrifugation (1200 rpm for 10 min). The supernatant was removed and the pellet resuspended in 0.2 ml PBS-Ca2+Mg2+ with 0,1% NaN3 paraformaldehyde. Twenty thousand labelling events were routinely accumulated and analysed for fluorescence on PAS flow cytometer (Partec, Mnster, Germany) using FloMax software. The results were statistically analysed using test ANOVA rang Kruskal-Wallis. Results: Results are showed in the table 2

Conclusion: In our study we have demonstrated that the mean number of NK cells expressing CD94 and CD158b not differ statistically in MM and NHL patients compared with normal donors.

MM		NHL		Control
Mean age/ Sex	Stage acc Durie and Salmon	Mean age/ Sex	Stage Ann Arbor	Mean age/ Sex
65 years/ 21Female 11 Male	I - 5 II - 8 III - 19	61 years/ 8 Female 11 Male	III - 1 IV - 18	59 years/ 5 Female 5 Male

	NK cells [G/l]	NK cells CD94+ [G/l]	NK cells CD94+NKG2A + [G/l]	NK cells CD158b+ [G/l]
NHL	0,359453	0,180631	0,117747	0,106208
MM	0,322615	0,186313	0,092499	0,124814
Control	0,172565	0,091928	0,081941	0,071086
p	NS	NS	NS	NS

Caption 1: Clinical data and results

**803** CYTOTOXICITY OF MONONUCLEAR CELLS (MNC) AND LYMPHOKINE ACTIVATED KILLER (LAK) CELLS AGAINST AUTOLOGOUS AND ALLOGENEIC TUMOR CELLS BY ACUTE LYMPHOBLASTIC LEUKAEMIA (ALL) IN CHILDREN

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Background: acute lymphoblastic leukemia may adversely affect the variety of immune functions. The possibility of recover cell immunity and augment cell cytotoxicity can provide therapeutic tool for tumor treatment.

Aim: to assess the cellular cytotoxic activity of blood/bone marrow MNC and LAK cells derived from children with ALL against allogeneic and autologous tumor cells.

Patients/methods: 38 patients (age 0-14 years, median 6,7) with ALL were enrolled in the study. MNC were separated from blood and bone marrow and were tested on both allogeneic blasts of K562 cell line and autologous lymphoblasts. Cytotoxic activity of MNC was assessed in acute period of disease before any treatment as well as after induction chemotherapy in remission. LAK cells were obtained in remission by in vitro incubation of MNC with interleukin-2 and were tested on the same target cells. Additionally, cytotoxicity of LAK cells from healthy volunteers was measured on K562 cell line and ALL patients' tumor cells. MTT was used to assess cytotoxic activity. Results: cytotoxicity of blood MNC against K562 line cells increased from 28,7% initially to 36,6% in remission (from 20,2% to 31,9% for bone marrow MNC, respectively). Blood MNC cytotoxicity against autologous blasts increased from 22,8% in acute period to 25,4% in remission (from 14,9% to 22,9% for bone marrow MNC, respectively). LAK cell cytotoxicity was 26,9% by testing against allogeneic tumor cells and 49,1% - against autologous blasts. Cytotoxic activity against K562 cell line as well as against autologous tumor cells had negative correlation (p<0,05) with age of patients and initial white blood cell count. Cytotoxicity of LAK cells obtained from MNC of healthy volunteers was 72,3% in test against tumor cells from patients with ALL. Conclusions: cytotoxicity of blood and bone marrow mononuclear cells is decreased in acute period of ALL and becomes significantly higher in remission. MNC cytotoxicity against allogeneic tumor cells is higher then that against autologous ones. It could be due to low susceptibility of autologous blasts to effector cells and due to immunosuppressive effects of tumor cells. MNC cytotoxic activity can be augmented by generation of LAK in presence of interleukin-2.

In comparison to ALL patients LAK cells from healthy volunteers are significantly more cytotoxic against allogeneic blasts.

#### 804 IMMUNOPHENOTYPICAL FEATURES OF B-CELL CHRONIC LYMPHOCYTIC LEUKEMIA

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**Background.** In the past years the immunophenotyping of leucocytes has won a central place in the diagnosis of chronic lymphocytic leukemia (CLL). But immunophenotype in CLL is usually heterogeneous and few markers have an important prognostic significance.

The aim of the study was to investigate immunophenotypical features of B-CLL and evaluate the prognostic power of some molecules.

**Material and methods.** The study included 180 B-CLL pts (M/F: 96/84), average age was 58 yrs (age range 38-75 yrs). Immunophenotypical studies were performed in peripheral blood smears using monoclonal antibodies 'DAKO' (Denmark).

**Results.** We divided our pts into 2 groups. Pts of group 1 (62/180 pts) were characterized by typical CLL antigens: CD5+, CD19+, CD20+, CD22+, HLA-DR+, CD23+, CD10-, sigslow. Pts of group 2 (118/180 pts) among typical for CLL antigens had activation antigens: CD11c, CD11b, CD25, CD38. The number of CD38-positive cells more than 30% was correlated with progressive course of the disease. The percentage of CD95-positive cells was significantly lower in CLL pts when compared with healthy individuals ( $p=0,002$ ). Presence of activation antigens was significantly associated with low percentage of CD95+ cells. The percentage of CD95+ cells was correlated with stage of CLL and type of bone marrow infiltration by CLL cells. All pts received CT with fludarabine. We compared response to CT and immunophenotypical features of CLL. In group of pts with atypical immunophenotypical features overall response rate was significantly lower compared with ones without atypical immunophenotypical features (58% and 88%, respectively).

**Conclusion.** Our results show that immunophenotypical features may be used as prognostic factors of course of the disease and efficiency of therapy.

#### 805 DEPRESSION/ANXIETY SYMPTOMS AND NEUROTICISM IN PATIENTS TREATED DUE TO HAEMATOLOGIC CANCERS

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**BACKGROUND:** Haematological treatment is associated with excessive distress due to severe life consequences of the illness and due to side effects of cytostatics. It is a cause of anxiety or depressive states in vulnerable persons.

**AIM:** The purpose of the study was to determine relation between neuroticism, distress and severity of depressive/anxiety symptoms in patients treated due to leukaemia and lymphoma.

**METHODS:** 45 patients with leukaemia or lymphoma, 46 treated due to other internal diseases and 45 healthy persons were assessed. The following research instruments were used: the Eysenck Personality Questionnaire (EPQ-R), the General Health Questionnaire (GHQ-30), criteria scales (ICD-10) for depression and anxiety.

**RESULTS:** the two groups of patients differed significantly from control group in scores of depression, anxiety and distress (GHQ). Differences in neuroticism level were small and not relevant statistically. The group with haematological illness had higher score of anxiety than the group other internal illnesses. The difference depended on psychic symptoms of anxiety, the score of somatic symptoms of anxiety was similar in all the groups. The level of neuroticism was similar in all the groups. It correlated with depression and anxiety scores in the groups of haematological patients (Pearson product - moment correlation  $r = 0.59$  and  $0.58$  respectively), and in the groups of other internal patients ( $r = 0.54$  and  $0.54$ ) but not in the control group ( $r = 0.1$  and  $0.15$ ).

**CONCLUSION:** The groups of haematological patients have higher, depressive and anxiety scores than controls and slightly higher than other patients with internal diseases. This is result of psychological stress coming from awareness of being sick and biological stress coming from and illness itself and from medication. Neuroticism score is the measure of stable personality trait and is not close related to symptoms nor stress. So neuroticism score could be a predictor of vulnerability to depressive and anxiety states in the course of internal illnesses.

#### 806 THE COMPARISON OF SPONTANEOUS LDH RELEASE ACTIVITY FROM CULTURES PBMC WITH SERA LDH ACTIVITY IN NON-HODGKIN'S LYMPHOMA PATIENTS

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Based on consideration that intracellular characteristics of lactate dehydrogenase (LDH) enzyme are very sensitive indicators of the cellular metabolic state, aerobic or anaerobic direction of glycolysis, activation status, malignant transformation, as well as membrane damage following cell death process, aim of this study was to correlate values of the spontaneous LDH release from circulated PBMC with their sera LDH activity in 43 different subtypes of lymphoma. The diagnosis of NHL patients was based on histological proven of the lymph node and bone marrow biopsy for appropriate patients, while clinical staging was performed according to the Ann Arbor system based on combination of clinical routine examination, blood and ultrasound analyses, chest ray and computerized tomography (CT) scan. The spontaneous LDH release after cell separation and 2h cultures of PBMC (at concentration 8, 4 and 2 x 10<sup>6</sup>/ml of culture medium) was determined by spectroscopic methods using substrate mixture on the micro-titer plate reader (Behringer EL-311, Germany) expressed as changes in absorbance at 492-630 nm. The results display that patients in advanced clinical stage (III and IV) have a significantly increase of sera LDH activity ( $p<0.05$ , Mann-Whitney U-test) in comparison to those in early stage (I and II). However, mean values for sera LDH activity, in low, intermediate and high grade malignancy in early stage (I and II) display mean values of LDH which is no significantly differ ( $p>0.05$ , Mann-Whitney U-test) in comparison to reference values (320 U/ml) although, some individual patients have elevated sera LDH activity. The investigation of spontaneous LDH release activity from cultures PBMC, expressed as changes in absorbance/min is a significantly differ among all observed groups based on histology and clinical stage ( $p<0.01$ , Kruskal-Wallis ANOVA). In addition, there are a significant positive correlation between spontaneous LDH release determined from cultures PBMC and serum LDH level in individual NHL patients ( $n=43$ ,  $r=0.493$ ,  $p=0.001$ ). Based on obtained data, we conclude that the evaluation of the spontaneous LDH release from cultures cells appears to be an additional parameter that correlates with particular subtypes and forms of lymphomas and, together with other findings may aid in their diagnosis, especially in patients with early stage of disease.

#### 807 AUTOIMMUNE HEMOLYTIC ANEMIA IS NOT MORE FREQUENT IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA TREATED WITH FLUDARABINE

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**Background:** Autoimmune hemolytic anemia (AHA) is a frequent event (10-20% of cases) in Chronic Lymphocytic Leukemia (B-CLL) and can appear at any time during the course of the disease. The mechanisms causing production of antibodies in B-CLL are not fully understood, some studies asserting the higher frequency of this one in patients treated with fludarabine.

**Aim:** Our study has a retrospective character wishing to evaluate the relation between LLC and AHA considering the therapy with fludarabine.

**Methods:** Between 1987 and 1999, AHA was observed at our institution in 25/165 (15,15%) patients with B-CLL (15 men, 10 women); median age 59 years, range (21-74).

**Results:** AHA was observed at times ranging from diagnosis to 68 months from diagnosis; in 24% patients before treatment initiation and in 76% after. In the later cases, 47,36% patients had received chemotherapy with chlorambucil and prednisone, 31,57% followed CVP (cyclofosamide, vincristine, and prednisone) and 21,05% had received fludarabine. There are not significant differences in the incidence of the AHA occurrence at the three groups of patients. The low hemoglobin value observed at onset of AHA was 5,2 g/dL (range 4,2-8,6 g/dL) but there are not important disputes between the lot of patients treated with FAMP (mean 6,3 g/dL) and the ones treated with alkylating drugs (mean 4,9 g/dL). The direct antiglobulin test was positive with anti IgG + anti C3d antiserum in 72% patients; in one (4%) patients with anti IgG + anti IgA + C3d antiserum; in 16% patients with anti C3d antiserum. All the patients undergoing treatment with fludarabine belong to the first lot but again the significant limit hasn't been attained. Only 24% cases required

packed red blood cell transfusions, two belonging to the group treated with fludarabine. All the patients were treated with corticosteroids (PDN 1mg/kg/day for up to three weeks), as for the lot treated with fludarabine this one was interrupted and switched to another antineoplastic therapy. Complete hematological response to AHAI was observed in 80% cases, 16% patients had partial response and 1 (4%) patient died of hemolytic crisis (fludarabine group). 20% of complete responders had AHAI relapse. Splenectomy is performed in 12% patients in two cases for multiple relapses after PDN and chemotherapy and one for incomplete response, none belonging to the group treated with fludarabine. Other three patients had received PDN in low doses for three to six months (between chemotherapy) for incomplete response of AHAI. Overall survival of the patients was 46 months from diagnosis of malignancy. Conclusions: Our data suggest that AHAI is more frequent in previously treated patients, with progressive B-CLL, than in untreated patients. AHAI had a low incidence in-patients treated with fludarabine without presenting important differences comparing with the rest of the patients with LLC and AHAI.

**808 THE EFFICIENCY OF SPLENECTOMY IN PATIENTS WITH IDIOPATHIC THROMBOCYTOPENIC PURPURA (IPT) RESISTING TO CORTICOTHERAPY**

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Background: Splenectomy is the second therapeutical line in-patients with IPT after failure of steroids or after 2-3 relapses in 6 to 12 months. The postsplenectomy rate response is between 65-75% in most of the literature studies.

Aim: The aim of this work is to evaluate the efficiency of splenectomy at the level of our lot of patients with IPT resisting to corticotherapy.

Methods: Our lot consists of a number of 56 patients with IPT diagnosed beginning with the year 1983. The median age was that one of 28 years old. (12) 21,42% of the patients belong to the male sex. The platelet count at the presentation at the time of splenectomy, the sex, the age, the months of evolution before surgery, the number of previous relapses, response and number of relapses after surgery were evaluated. CR was defined as normal platelet count for  $\geq 1$  month on no treatment and without relapse and PR as platelet count  $\geq 50 \times 10^9/L$  at least 1 month after splenectomy and no criteria for CR.

Results: 16 (28,57%) of patients with IPT were splenectomized. The platelet count at the time of the surgery indication varied between 12.000 and 38.000/mm<sup>3</sup> platelets with an average of 21400 mm<sup>3</sup> of platelets. 4 (25%) of the splenectomized patients were male and 12 (75%) female. Median age at diagnosis: 26 years (14-54). Months from diagnosis until splenectomy was 28,7 (7-210). Indication of surgery was: 7(43,75%) patients were refractory to previous treatment and 9 (56,25) patients presented different number of relapses (3-4). There was no death after the surgery and morbidity is materialized in complications like: one case with left side pleurisy, a subphrenic abscess and two cases of the thrombophlebitis of the leg. In our series, total response rate, including CR or PR was achieved in 81,25% of the patients: 8 (50%) CR and 5 (21,75%) PR, with a median following time of 88 months (12-250). No-responding patients underwent the immunosuppressive therapy with good results in two of the three cases.

Conclusions: The indication of splenectomy in our patients with IPT has a percentage of 28,57%. Total response rate (CR+PR=76,18%) to splenectomy seems to be similar to that reported in the literature, although a lower CR rate is observed.

**809 FOUR CYCLE OF COPP/ABVD FOLLOWED BY LOW DOSE INVOLVED FIELD RADIATION THERAPY (LDIF RT) ARE INAPPROPRIATE IN UNFAVOURABLE SUPRADIAPHRAGMATIC CLINICAL STAGES I-II HODGKINS DISEASE**

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Background. The patients with Hodgkin disease(BH), stage I and II have a high rate of complete remission and a long time survival. The identification of some risk factors in this group of patients allowed different therapeutical approach.

Aim. Our study has retrospective character and wants to emphasize that four cycles of COPP/ABVD plus LDIF RT represent an inappropriate therapeutical modality for unfavourable supradiaphragmatic clinical stages I and II Hodgkin's disease.

Methods. The study group includes 63 patients with HD stage I (9 patients) and stage II (54 patients), except bulky and II B. Nodular sclerosis is present in 65.07% of cases. The mean age is 37 years and males are slightly predominant (34/29). The therapy consists of four cycles of COPP (before 1994) or ABVD combination chemotherapy followed by LDIF RT (24-32 Gy) in patients with complete response (CR). Patients with stable or progressive disease after four cycles of chemotherapy were switched to extended field radiotherapy (36-40 Gy). Minimum follow-up was 2 years, with a median of 51 months.

Results. From the 63 patients with BH in stage I and II with supradiaphragmatic disease, 31,74% present at least one unfavorable prognostic factor: the age  $\geq 50$  years, stage II with more than four involved areas, stage A+VSH  $\geq 50$  mm/h or stage B+VSH  $\geq 30$  mm/h. CR after polichimiotherapy has been attained in 40 cases (93,02%) for BH in stage I and II with supradiaphragmatic disease and favorable prognostic and only 75% of the patients with Hodgkin disease stage I and II with unfavorable prognostic (Fisher exact  $p=0,01$ ). It means that the proposed protocol for BH in stage I and II, non bulky was completed for only 75% of the patients with BH stage I and II with unfavourable prognostic. The association of the extended radiotherapy increases the CR rate to 97,67% for the first lot and to 85% for the lot with risk factors (Mantel Haenszel  $p=0,05$ ). The survival rate free of the disease after 4 years was of 95,23% for the lot of patients with favourable prognostic and of 76,47% for those ones with risk factors (Mantel Haenszel  $p=0,03$ ). None of the patients with BH stage I or II and risk factors undergoing extended radiotherapy had a relapse (Fisher exact  $p=0,04$ ).

Conclusions: The differences of therapeutical response to the applied protocol are significant between the two lots: the patients with BH with unfavorable prognostic present a lower rate of complete remissions after the 4 cures of COPP/ABVD, the relapse rate at 4 years is higher and all these patients belong to the lot undergoing LDIF RT. It means that four cycles of COPP/ABVD followed by LDIF RT is not enough for unfavorable supradiaphragmatic clinical stages I-II Hodgkins disease.

**810 DISSEMINATED INTRAVASCULAR COAGULATION AND SERUM VEGF LEVELS IN PATIENTS WITH ACUTE LEUKEMIA**

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Background: Laboratory findings of disseminated intravascular coagulation (DIC) are common in patients with acute leukemia. Tissue factor is a major activator of pathologic coagulation process in DIC. Tissue factor antigen is elevated in patients with acute leukemia and DIC. Recent studies have shown that tissue factor may be involved in tumor angiogenesis and metastasis and is implicated in regulation of vascular endothelial growth factor (VEGF) - a most important angiogenic factor.

Aims: To determine laboratory parameters of DIC in acute leukemia patients and to correlate them with serum VEGF levels and patient survival time.

Methods: 35 adult patients with acute leukemia were studied (3 with acute lymphoblastic leukemia, 32 with acute myeloblastic leukemia). The following coagulation tests were performed on diagnosis, before induction therapy, using routine laboratory techniques: Prothrombin time (PT), activated partial thromboplastin time (PTT), fibrinogen, platelet count, thrombin time (TT), D-dimer, fibrinogen split products (FSP). Serum VEGF level were assayed concomitantly using a commercial quantitative sandwich enzyme immunoassay technique.

Results: Abnormal PT was found in 16(46%) patients, prolonged PTT in 1(2.8%) patient, decreased fibrinogen level in 2(5.7%) patients, D-dimer was elevated in 16 patients (46%) and FSP in 13 (37%). The mean serum VEGF level was 45 pg/ml (range 4.45-139). A borderline correlation was found between PTT and log serum VEGF level ( $p=0.086$ ) and fibrinogen and log serum VEGF level ( $p=0.097$ ). No correlation was found between serum FEGF level and PT, TT, D-dimer, and FSP levels. Furthermore, no correlation was found between VEGF levels and patients survival time.

Conclusions: Coagulation abnormalities consistent with DIC are prevalent at diagnosis in acute leukemia patients (37-46%). No correlation was found between them and serum VEGF levels, suggesting that released tissue factor, reflected by the onset of DIC in patients with acute leukemia, does not trigger angiogenesis in these patients.

### 811 THE HAEMOPHAGOCYTTIC SYNDROME (HPS) A CLINICOPATHOLOGIC STUDY OF 12 PATIENTS IN AN ASIAN POPULATION

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#### Background:

HPS is a clinico-pathologic entity characterised by systemic proliferation of non-neoplastic histiocytes showing phagocytosis of haemopoietic cells, resulting in blood cytopenia. It has been associated with a variety of infections, collagen vascular diseases and malignancies, especially lymphomas.

#### Aims:

The clinical spectrum and outcome of 12 cases of HPS in Singapore between 1998-2003 are reviewed.

#### Methods:

The investigation is a retrospective study of the clinical characteristics and outcomes of 12 patients with HPS diagnosed on bone marrow aspirate over a 5-year period.

#### Results:

HPS affected both sexes of a wide age range. 8 cases were associated with malignant lymphoma, 2 were associated with infections including 1 case of disseminated tuberculosis, 1 patient had acute leukaemia and 1 had no obvious underlying disease found. All patients presented as cases of pyrexia of unknown origin with high spiking fever, cytopenia, abrupt drop in blood counts, and deranged liver function and coagulation profiles. 10 including all 8 lymphoma cases died of acute diseases and only the 2 patients with infections are still alive. All lymphoma cases had a systemic presentation, poor outcomes and lymphoid infiltration of the bone marrow at presentation, although significant lymphadenopathy were disappointingly rare. HPS associated with viral infection is uncommon as compared with western populations.

#### Summary:

A review of the literature revealed that most cases of HPS have fulminant courses. The 8 cases of lymphoma had a median survival of only 47.3 days from onset of symptoms. As tumour masses indicative of lymphoma were not striking in most of the lymphoma cases, bone marrow studies appear to be of great value for the diagnosis of HPS-associated lymphoma.

#### Conclusion:

HPS is an uncommon disorder. A vigorous search for an underlying malignancy or infection is warranted once diagnosis is made. It may obscure the diagnosis of an underlying and treatable infectious disease. An early diagnosis and prompt initiation of chemotherapy may improve the prognosis of HPS-associated lymphoma.

### 812 NON HAEMATOLOGICAL MALIGNANCY MASQUERADING AS ACUTE LEUKAEMIA: THE LIMITATIONS OF IMMUNOPHENOTYPING

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#### Background:

In the UK, guidelines for the diagnostic immunophenotyping of haematological malignancies (Bain et al 2002) have been produced by the British Committee of Standards in Haematology (BCSH). A stepwise approach is undertaken, with morphological assessment and the primary antibody panel used to establish lineage specificity. This will in turn determine the choice of secondary panel antibodies. If plasma cell differentiation is suspected, the secondary panel includes detection of cytoplasmic (cyt) immunoglobulin (Ig) heavy and light chains, cyt CD79a and surface CD138.

#### Aims:

To highlight the pitfalls of immunophenotyping, despite adherence to the BCSH guidelines, when dealing with a non-haematological malignancy.

#### Case report:

A 56 year-old man presented with a 1 month history of malaise, lethargy, easy bruising, epistaxis and 10kg weight loss. His past medical history was unremarkable. He was taking no medications. He was an ex-smoker (stopped 20 years ago) of 10 pack years. Although he worked as a building site manager, there was no known exposure to toxic chemicals, including asbestos. The significant findings on examination were: cachexia, bruising on the trunk and limbs, oral candidiasis, a craggy mass in the right upper quadrant, proven on imaging to be hepatomegaly.

Haemoglobin measured 8.0g/dL, WCC 8.7 x 10<sup>9</sup>/L and platelets 50 x 10<sup>9</sup>/L. A blood film showed blasts and myeloblasts accounting for 1% of white cells. A bone marrow aspirate showed normal marrow elements effaced by sheets and clusters of what appeared to be small blasts. The patient was referred to our care with a presumptive diagnosis of acute lymphoblastic leukaemia (ALL).

#### Immunophenotyping results:

The primary panel revealed a CD13+, CD117+ , CD45-, HLA-DR- population, which was negative for B- and T-lineage antigens, as well as cytMPO and nTdT.

The secondary panel showed the cells to be SmlgM+, cytlgM+, intracellular-k restricted, CD138+ and CD56+.

#### Interpretation of data

The presentation and cell morphology were consistent with an acute leukaemia. However, the primary panel excluded the possibility of ALL, while CD45 and HLA-DR negativity suggested a plasma cell dyscrasia or a non-haematological malignancy, rather than AML. Overall, the immunophenotype was strongly suggestive of a plasma cell dyscrasia - CD45-, CD56+, CD117+, CD138+, SmlgM+, cytlgM+, HLA-DR-. Indeed, the strong cyt-k restriction would be regarded by the BCSH guidelines as being plasma cell lineage-specific.

#### Final diagnosis:

The trephine biopsy was hypercellular, with diffuse involvement by non-haematological cells staining for NCAM, but negative for LCA and MN116. A CT scan of the chest revealed a right hilar mass. A diagnosis of bronchial small cell carcinoma was made.

#### Conclusion:

This case highlights:

- 1) Non-haematological malignancy may present clinically and morphologically as acute leukaemia.
- 2) The limitations of immunophenotyping, which suggested a plasma cell dyscrasia.
- 3) Cytoplasmic light chain restriction is not always lineage specific for plasma cells.
- 4) Unusual clinical findings (hard, irregular hepatomegaly) and CD45 and HLA-DR negativity were indications for the need to exclude a non haematological malignancy.

### 813 MYELOBLASTOMA AS INITIAL MANIFESTATION OF ACUTE MYELOID LEUKEMIA

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**Background:** Myeloblastoma (chloroma, granulocytic sarcoma) with no demonstrable abnormalities in the peripheral blood (PB) and bone marrow (BM) is a rare initial manifestation of acute myeloid leukemia (AML). The majority of patients (pts) present with AML very soon after myeloblastoma diagnosis.

**Aims:** We are presenting the analysis of clinical and laboratory data for 5 pts with extramedullary AML (myeloblastoma).

**Methods:** The diagnosis of myeloblastoma was established by immunohistochemical investigations (IH) (CD34+,CD117+,MPO+). BM analysis included morphology, immunophenotype and cytogenetic studies.

**Results:** Five pts (male 2, female 3; age : child 7 yrs, adults 25-66 yrs) presented with myeloblastoma of the female genital tract ( uterus- 1 pt, ovary with abdominal lymph nodes and peritoneal tissue- 1pt ), cervical lymph nodes (1 pt), subcutaneous tumor in the parietal region of the head (1 pt) and orbital tumor ( 1 pt ). At the moment of myeloblastoma diagnosis all pts had normal PB counts, with normal BM investigations (mentioned above) done in 2/5 pts. All pts were treated with radical surgery for tumor. But, 2-12 months (Me 7,5), after operation there were signs of AML in PB and BM in 4/5 pts ( 2 pt M2 and 2 pt M4 FAB type, with pathologic karyotype in only one M4 pt- inv16 ) without extramedullary tumors of any site. AML was diagnosed even in pt treated with one cycle of AML induction chemotherapy after operation , but 12 months after initial diagnosis. Pt with uterus myeloblastoma (66 yrs) is still alive (9 months) after radical operation, without chemotherapy and without AML signs. AML treatment was successful in 2/4 pts, with complete remission (duration 2 and 8 months) and overall survival of 5 and 18 months. Two pts died due to resistant AML (7 and 17 months after myeloblastoma diagnosis).

**Conclusions:** Our experience confirms the significance of IH investigations for the myeloblastoma diagnosis, with complete BM studies, followed

by intensive AML chemotherapy in young pts, due to bad prognostic influence of this extramedullary AML

#### **814** QUALITY OF LIFE DURING THERAPY FOR AGGRESSIVE NON-HODKINS LYMPHOMA IN PATIENTS WITH DIFFERENT AGE

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**Background:** Although patients age is one of the recognized prognostic factors in aggressive Non-Hodgkins Lymphoma (NHL) and the choice of treatment is often modified due to it, it is not stated yet if the patients need a Quality of Life (QOL) evaluation with age-specific instrument.

**Aims:** The aims of this study are to evaluate the impact of the lymphoma characteristics on the QOL of patients and to see if it is dependant on their age.

**Methods:** A group of 109 patients (median age 59 years, range 18-83) with aggressive NHL is presented, as well as its two subgroups of different age, separately: 58 patients younger than 60 years and 51 patients older than 60 years. The disease characteristics and the patients QOL have been assessed using the International prognostic index (IPI), age-adjusted IPI (aaIPI) (Shipp, 1995) and the QLQ-C30 (Aaronson, 1993).

**Results:** The majority of the patients (33,0%) and the majority of the elders (33,3%) had high IPI, while the younger ones had the high-intermediate IPI more frequently (29,3%). In the group analyzed as a whole, patients with the high IPI, experienced all their functional abilities as significantly lower, compared to those of better prognosis. The exception was their cognitive functioning (CF), that did not depend on the index ( $p=0,12$ ). The patients personal assessment of the most of their physical disabilities (fatigue, nausea, pain, dyspnoea, appetite loss) also depended on the IPI ( $p<0,01$ ). When evaluating the subgroup of patients younger than 60 years, the only functional abilities found independant on the aaIPI were the CF ( $p=0,16$ ) and the social functioning (SF) ( $p=0,09$ ). The half of the investigated physical disabilities (fatigue, dyspnoea, appetite loss, insomnia) were experienced as significantly dependant on the aaIPI by younger patients ( $p<0,01$ ). On the contrary, the only QOL components experienced as dependant on the aaIPI by the elders, were the SF ( $p=0,04$ ), the global assessment of QOL ( $p=0,008$ ) and the fatigue ( $p=0,01$ ).

**Summary:** The changes in the physical health lead to the persons experience of lowering own functioning abilities and global QOL but the data suggest that the perception, the experience and/ or the communication of QOL seem to be age-dependent. An age specific instrument for the QOL assessment in the NHL patients seems to be needed.

#### **815** CLINICAL EVALUATION OF ONCE WEEKLY DOSING

OF EPOETIN ALPHA IN MULTIPLE MYELOMA PATIENTS: IMPROVEMENT IN HEMOGLOBIN ARE SIMILAR TO THREE-TIMES-WEEKLY DOSING

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**Introduction.** The prevalence of anemia in patients with multiple myeloma is greater than 80%. Erythropoietin (EPO) leads to achievement and maintenance of high haemoglobin levels, which are of considerable prognostic significance in patients with multiple myeloma. The efficacy of single, weekly doses of EPO has been recently confirmed.

**Purpose** of this study was to evaluate the clinical effects of single, weekly doses of EPO in anemic patients affected by multiple myeloma (MM).

**Patients and Method.** We studied 43 anemic MM patients, 23 men and 20 women, who were diagnosed and treated in our clinic during the past five years. Their mean Hb level before EPO treatment was 10.5 gr/dl (range: 6.3-12 gr/dl). Patients were randomized in two groups and EPO was administered subcutaneously, at a dose of either 10.000 IU three times a week or 40.000 IU once weekly. Hb level response was evaluated 4 weeks and 3 months after treatment initiation. A major response was regarded an increase of untransfused Hb levels equal or greater than 2 gr/dl, while a minor response was regarded an increase in Hb levels of at least 1 gr/dl. No response was defined as a response less than a minor response.

**Results.** Twenty-six patients received EPO at a dose of 10.000 IU three times a week. According to defined response criteria, at 4 weeks after treatment initiation, 19 patients (73%) responded to EPO treatment. Eight patients (30.8%) attained a major response, while 11 patients (42.2%)

attained a minor response. Seven patients (27%) did not respond to EPO treatment. Three months after treatment initiation, Hb levels remained stable or slightly raised in 7 major responders, while 1 patient presented with decreased Hb levels, due to disease progress and 9 minor responders attained major response. The remainders required an increase of EPO dose to 150 U/kg 4 times a week. Seventeen patients received EPO at a dose of 40.000 IU once weekly. At 4 weeks after treatment initiation, 12 patients (70.6%) responded to EPO treatment. Six patients (35.3%) attained a major response, while 6 patients (35.3%) attained a minor response. Five patients (29.4%) did not respond to EPO treatment. Three months after treatment initiation, Hb levels remained stable or slightly raised in 5 major responders, while 4 minor responders attained major response. The remainders required an increase of EPO dose to 150 U/kg 6 times a week. Between the two groups, compliance was equal but convenience was superior in the group receiving the single weekly dose. **Conclusions.** Our study shows significantly increased and sustained response of anemic MM patients to recombinant human erythropoietin treatment and suggests that 40.000 IU of EPO given once a week is at least as effective as the more frequent three times a week administrations of the drug usually employed in MM patients and optimizes patients convenience.

#### **816** QUALITY OF LIFE IN PATIENTS WITH AGGRESSIVE NON-HODKINS LYMPHOMA AND THE THERAPY OUTCOME

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**Background:** The gain in the Quality of Life (QOL) is an attainable aim when aggressive Non-Hodgkins Lymphoma (NHL) patients are treated. It is important to know which QOL domains depend on the therapy outcome.

**Aims:** The aims of this study are to see which are the QOL domains that differ significantly between responders and non- responders and if those differences last.

**Methods:** A group of 109 adult patients with aggressive NHL is presented. The patients QOL has been assessed using the QLQ-C30 (Aaronson, 1993) and The Experience of Quality of Life Questionnaire (EQLQ) (Berger, 1989) at the time of diagnosis, the therapy evaluation and six months later. EQLQ measures the patients perception of his health, his life, his family and social relationship and orientation towards the future.

**Results:** Patients that achieved complete remission (CR) assessed almost all the components of their QOL as better when compared to patients with no remission (NR) and they experienced less physical disabilities. The experience of family relationship (EFR) was the only QOL domain that did not differ in the two subgroups ( $p=0,54$ ). In the sixth month of the follow-up neither the experience of social relationship ( $p=0,11$ ) nor EFR ( $p=0,63$ ) differed between them significantly. At that time of evaluation, patients in remission assessed their functional abilities as better comparing to non-responders, but the differences between them were of minor statistical significance comparing to the estimations made six months before. As for the physical symptoms, there were no differences in the patients experiences regarding their hematological status any more.

**Summary:** The results suggest that the family coherence did not depend on the therapy outcome. This is important because of the possibilities that doctor-family cooperation means for the treatment. Patients in CR have more difficult social tasks; some domains of functioning (like role and cognitive) may get better in spite of lymphoma resistance; non-responders may have more intensive medical care and attention and the late toxicity effects have their impact on all the patients. These are the possible explanations for the fact that QOL of responders and non-responders seem to become more similar during the follow-up.

#### **817** CHEMOTHERAPY IMPACT ON GASTROINTESTINAL SYSTEM'S MUCOSA ABSORPTION IN PATIENTS WITH ACUTE MYELOBLASTIC LEUKEMIA (AML)

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**Background.** The role of leukemic cells and the chemotherapy impact on the gastrointestinal system's mucosa is not entirely clear. It is still unknown whether patients with AML have small intestinal malabsorption, which also can be changed by antileukemic therapy or whether that

malabsorption might have impact on patients' malnutrition. Neoplastic cachexia in leukemic patients has been observed very often especially in those cases with high expression of interleukin-6 (IL-6) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ).

The aim of the study was to assess an ability to absorption in small intestine by D-xylosis test in AML patients before and after induction chemotherapy and compare with body mass index (BMI) and serum concentration of IL-6 and TNF $\alpha$ .

**Patients and methods.** Twenty-three patients with AML we enrolled in the study: 11 females and 12 males aged 25-77, mean 48 years. According to FAB classification: 1 patient represented AML-M0, 4 patients- M1, 8 patients- M2, 9 patients 'M4 and 1 patients-M6. All patients received standard chemotherapy including farnorubicine and Ara-C. D-xylosis tests were performed before and 14-18 days after first course of chemotherapy. Concentration of IL-6 and TNF- was measured by ELISA method in the same time.

**Results.** There was no statistical difference between D-xylosis elimination, BMI and concentration of IL-6 and TNF- $\alpha$  before and after chemotherapy. Concentration of IL-6 was statistically higher before than after treatment (22.344.1pg/ml vs. 6.89.3pg/ml;  $p=0.01$ ). There was no difference between TNF- $\alpha$  concentration in patients before and after treatment.

**Conclusion.** The data indicate that further examination on the chemotherapy role on malabsorption should be performed in patients with AML.

#### **818 CLINICAL COURSE OF CML IN PATIENTS WITH COMPLEX PH CHROMOSOME TRANSLOCATION TREATED WITH IMATINIB THE ROLE OF CONVENTIONAL CYTOGENETICS AND RESIDUAL DISEASE MONITORING USING REAL-TIME QPCR**

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**Background:** Chronic myelogenous leukemia (CML) takes a natural course with evolution from chronic (CP) towards acceleration phase (AP) and blast crisis (BC) characterised by fatal outcome. Introduction of imatinib, and the development of reliable methods for quantitative PCR (qPCR) have significantly influenced the course of CML. Treatment with imatinib induces major or complete cytogenetic remissions in more than 40% of patients resistant or intolerant to IFN alpha. qPCR is frequently used for monitoring patients in addition to or instead of conventional cytogenetics. Additional chromosomal abnormalities detected at diagnosis or arising during the CML treatment may have a prognostic value, and could be undetected when using qPCR alone in the assessment of residual disease during therapy.

**Aims:** to compare the course of CML in patients with complex and 'classical' Ph translocation treated with imatinib, and evaluate the role of qPCR and conventional cytogenetics in monitoring of residual disease in these patients.

**Methods:** Forty three patients treated with imatinib for CML in different stage were prospectively followed in three months intervals with RT-PCR, qPCR and karyotyping for the follow-up of 34 (mean 13) months. Comparisons were made between qPCR and karyotyping results from the bone marrow. Sokal index, Euro score, treatment response and progression-free survival was assessed.

**Results:** We detected complex Ph chromosome in 14% (6 out of 43) of patients at start of imatinib therapy. After 3 months of treatment 5 out of 6 patients (83%) (all from CP group and one from the BC group) achieved complete hematological response (CHR). One patient with CP achieved CCyR after 6 months of treatment with more than 2 log reduction of BCR-ABL transcripts in qPCR, being positive in RT-PCR. In one patient there was a 2 log reduction of BCR-ABL transcript in qPCR despite persisting of the complex Ph chromosome in the conventional cytogenetics. Two patients died because of CML progression; one from the CP and one from the BC group. In two patients (one with CP, one with BC) we were able to detect simultaneously p210 and p190 BCR-ABL transcripts by RT-PCR. The analysis of the Sokal and Euro score, the response rate to imatinib, clinical course and PFS, didnt differ significantly form patients with 'classical' Ph chromosome.

**Summary/Conclusion:** The course of CML in our patients with complex Ph seems to be similar to patients with 'classical' Ph, however the clear conclusion regarding the risk profile cannot be made because of their small number. Our observation of 2-log BCR-ABL transcript reduction in qPCR in patient with residual complex Ph is in accord with other studies reporting the occurrence of clonal cytogenetic abnormalities in the Ph-negative cells, which appeared after suppression of the Ph-positive clone by imatinib, and supports number of data suggesting that cytogenetics

should not be completely replaced by qPCR. False reassurances of successful imatinib treatment by qPCR can result in disease progression and delay of patients referral for alternate therapies.

#### **819 -THALASSEMIA INTERMEDIA AND MALIGNANT LYMPHOMA: A REPORT OF TWO CASES**

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**Introduction.** Malignant lymphomas are rare among  $\beta$ -thalassemia patients. We describe two patients with  $\beta$ -thalassemia intermedia who presented with non-Hodgkin lymphoma and Hodgkins disease, respectively.

**Case reports.** We refer to a male and a female patient, 37 and 52 years of age, respectively. They both suffered from  $\beta$ -thalassemia intermedia and were splenectomized at the age of 14 and 21, respectively. Since then, they were both on a regular transfusion schedule of 2 units of red packed cells every 3 weeks, in order to maintain a pre-transfusion hemoglobin concentration of 9-10gr/dl, and were treated with desferoxamine for iron overload. The male patient had chronic hepatitis C infection and was on antiviral therapy with ribavirin and interferon- $\alpha$ . The patients were followed-up monthly, in the Thalassemia Unit of our hospital, with detailed history and clinical examination, complete blood count and laboratory tests for renal and liver function.

During a scheduled follow-up, in June 2003, the male patient presented with cervical, axillary and inguinal lymphadenopathy, persisting for more than 3 weeks, without co-existence of constitutional symptoms. Cervical lymph node biopsy revealed a marginal zone B-cell lymphoma. The clinical stage was IIIA.

The female patient was referred to the Thalassemia Unit in November 2003, with a left supraclavicular lymph node. Physical examination revealed the presence of bilateral axillary and inguinal nodes. Constitutional symptoms were absent. Supraclavicular lymph node biopsy showed lesions compatible with the non-classical Hodgkins disease of the nodular lymphocyte predominant subtype. The clinical stage was IIIA.

**Conclusion.** On reviewing the literature, only five cases of thalassemia and lymphoma are reported worldwide, thus making our cases the sixth and seventh report of this rare combination of diseases. The increase of mean survival in  $\beta$ -thalassemia patients due to the current medical facilities, the chronic blood transfusions, the state of altered immunological reactivity and the chronic infections may have an impact on the incidence of malignant lymphomas among these patients. Further studies are needed in order to understand the relationship between the two entities.

#### **820 AUTOLOGOUS STEM CELL TRANSPLANTATION FOLLOWING EFFECTIVE TREATMENT WITH THALIDOMIDE OF PATIENTS WITH MULTIPLE MYELOMA RESISTANT TO CONVENTIONAL CHEMOTHERAPY**

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**Background:** Thalidomide has proven to be effective in treatment of myeloma. It inhibits angiogenesis and has an immunomodulatory effect. The aim of this study was to assess the effectiveness of mobilization and collection of progenitor stem cells of haematopoiesis as well as haematological recovery following autologous transplantation of progenitor cells in patients with resistant multiple myeloma, effectively treated with thalidomide.

**Material and Methods:** Autologous transplantation (PBSCT) was conducted in 10 patients treated in our Department for multiple myeloma resistant to standard chemotherapy. 7 males and 3 females aged at average 55 yrs (range 42-64) were treated. The patients had the following types of MM: 4 IgG kappa, 2 IgG lambda, 2 IgA kappa, 1 IgA lambda and 1 IgD lambda. All the patients had reached the IIIA clinical stage according to Durie Salmon staging system. Positive response to treatment with Thalidomide (at least PR according to SWOG) was achieved in all patients. The initial dose of 200mg/d of thalidomide was increased to 400mg/d after 4 weeks of treatment. Administration of thalidomide was combined with dexamethazone at a dose of 40mg/d for 4 days every 28 days. After a period of between 8-24 weeks of treatment with thalidomide (approximately 17 weeks), when best results were achieved, patients were qualified for stem cells mobilization. Cyclophosphamide at a dose of 4g/m<sup>2</sup> and G-CSF (Neupogen) at a dose of 5 mgm/kg/day were employed in the course of mobilization.

**Results:** Mobilization was successful in all cases, 2-3 cytophereses were conducted at the average. The following results were obtained: