

treatment toxicity

560 LONG-TERM CARDIOPULMONARY TOXICITY IN PATIENTS CURED WITH COMBINED CHEMO-RADIOTHERAPY (CT-RT) FOR HODGKIN'S DISEASE: EVALUATION WITH EXERCISE TEST

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Background: Treatment for Hodgkin's disease can be curative for the majority of patients (pts); since most of them are less than 30 years of age at the time of diagnosis, cardiac and pulmonary sequels are of great concern. Therefore the aim of the present study was to investigate the cardiopulmonary response to exercise in pts treated with combined CT-RT and in continuous complete remission.

Material and methods: We investigated 126 pts suffering from Hodgkin's disease after a follow up of at least 5 years from the completion of the combined therapy. Sixty two pts had been treated with ABVD-RT, 40 with ABVD-MOPP-RT and 24 with VEBEP-RT. Median dose of RT to mediastinum was 36 Gy. Patients were submitted to respiratory function evaluation, 2D-Echocardiography before exercise and to the determination of cardiac output by acetylene rebreathing method before and during symptom limited exercise on cycloergometer using an incremental protocol.

Results: On the basis of respiratory function, we divided pts in three groups: Group 1: (72 patients) normal spirometry and transfer lung function for CO (DLCO); Group 2: (45 patients) normal spirometry and DLCO less than 80% of predicted; Group 3: (9 patients) total lung capacity and DLCO less than 80% of predicted. Patients of group 3 showed in comparison to patients of group 1 and 2 a lower tolerance to exercise, a lower oxygen consumption, an higher respiratory rate, a lower O2 pulse and a lower cardiac output per oxygen uptake. No patient had clinical symptoms or experienced toxicity severe enough to require treatment.

Conclusions: These data indicate and abnormal exercise physiology in patients with persistent pulmonary impairment especially when the reduction of DLCO is associated with decrease of total lung capacity. The lower exercise capacity seems to be due to a combination of decrease cardiac performance and an impairment of gas diffusion capacity with probably prevalence of cardiac impairment. Nevertheless cardiopulmonary dysfunction was minimal in fact in this series of pts curative combined RT-CT, had toxic pulmonary and cardiac effects which remained only at subclinical level.

561 ANALYSIS OF LONG TERM OUTCOME AND LATE TOXICITY IN HODGKIN LYMPHOMA SURVIVORS

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Background: Hodgkin lymphoma therapy (HL) can contribute to delayed toxicity. The purpose of this retrospective study was to evaluate long-term outcome of HL survivors.

Methods: The medical data analysis of 150 patients (pts) with HL treated in an oncological center in Poland between 1992 and 2005 has been performed. There were 80 females and 70 males, median age 31 years (range 15-69), and 110/150 pts (73.4%) in CSI/II, 40/150 pts (26.6%) in CSIII/IV. Half of the 150 pts presented B-symptoms. The most common pathology subtypes were NS (60%) and MC (23%). Chemotherapy (MOPP, MOPP/ABV or ABVD regimen) and radiotherapy (mantle-field or involved-field) were given to 138/150 (92%) pts with average of 6 cycles/patient, and to 108/150 (72%) pts with median 45 Gy respectively. Chemoradiotherapy received 96/150 pts (64%).

Results: CR achieved 122 pts (81%), PR 23 pts (15.3%), and ORR was 96.6%. With a median follow-up of 72 months, there were 24 relapses and 23 deaths (19 HL progression, 3 secondary cancer and 1 coronary heart disease). Five year DFS and OS were 78% and 92% respectively. Late toxicity/impairment of health were revealed in 62/150 pts (41.3%). There were: secondary amenorrhea in 30 women, musculoskeletal abnormalities in 26 pts (osteoporosis, spondyloarthritis, Perthes disease, Scheuermann disease, reumathoid arthritis), depressive syndromes (n=10), pulmonary fibrosis (n=9), polyneuropathy (n=5), hypothyreosis (n=4) coronary heart disease (n=3) and secondary cancer (n=7). Among these 7 malignancies there were: 1 osteosarcoma, 1 melanoma, 1 non-small cell lung cancer, 1 colon carcinoma, 1 cervical carcinoma, and 2 skin basal-cell carcinoma. A median time from the end of the treatment to development of the secondary malignancy was 8 years. The relative risk of the late toxicity/health impairment among pts treated with either initial chemotherapy alone or combined modality therapy was similar, and did not reach statistical difference (p=0.20).

Conclusions: Therapy of HL provides cure in more than 3/4 of our patients. In these patients, such treatment caused a substantial amount of variety health impairment, and even fatal diseases. This study indicates the need of a careful, long term medical surveillance in HL survivors.

562 LATE TOXICITY AND QUALITY OF LIFE (QOL) AFTER TREATMENT FOR HODGKIN DISEASE (HD): A GRUPPO ITALIANO STUDIO LINFOMI (GISL) COHORT STUDY ON 223 PATIENTS

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Background: Because of successful treatment, a large number of HD patients become long term survivors and remain at life-long risk for late sequelae that could impair QOL. Aims of this study were to assess late toxicity and to evaluate the QOL.

Patients and Method: GISL maintains a central database on characteristics, treatments, outcome and follow up (FU) of patients who entered clinical trial. For this retrospective study, we extracted data on 223 patients. To evaluate QOL patients were given a questionnaire with 21 items, evaluating different psychological spheres, including relational, affective, emotional and behaviour areas.

Result: 208 patients achieved complete response (CR); relapses occurred in 35 patients of which 16 obtained a 2° CR. After a median FU of 149 months, 168 patients are alive and 53 died: 22 for progressive disease, 14 for 2° tumours, 6 for cardiac disease, 3 for respiratory failure, 2 for infection and 6 for unknown causes. Two patients were lost at FU. Overall, late toxicity was observed in 82 patients of which 29 developed a 2° tumours and 51 non-malignant toxicity, including cardiac and pulmonary diseases, endocrinal dysfunction, fertility anomalies, gastric disturbances and infections. The evaluation of QOL is still ongoing and at this time 92 patients have filled out the questionnaire, principally reporting alteration of adaptation and relational spheres.

Conclusion: Late sequelae is an important concern, in particular because of the high number of 2° cancer and cardiac and pulmonary diseases. Further, although our data on QOL are still incomplete, they showed that side effects may heavily impact on QOL, worsening adaptation and relational spheres. An accurate evaluation of late sequelae and its impact on QOL is important in order to balance treatment efficacy and toxicity.

563 RISK OF SECOND CANCER IN PATIENTS WITH HODGKIN LYMPHOMA WHO RELAPSE AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION

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Background: The incidence of relapse, death and secondary cancers, was evaluated in pts with Hodgkin Lymphoma (HL) who underwent high-dose therapy and autologous stem cell transplantation (ASCT). Aim of the study was to assess the impact of these events on survival.

Methods: From March 1986 to August 2007, 107 pts with relapsed/refractory HL received high-dose chemotherapy supported by autologous bone marrow (20 patients), peripheral blood stem cells (85 patients) or both (2 patients). The preparative regimen to transplant was BCV (carmustine, vepeside, cyclophosphamide) in 52 patients and BEAM (carmustine vepeside, cytarabine, melphalan) in 55.

Results: Patient characteristics: female/male ratio 38/69; median age 31 years (16-62). Of 107 patients, 101 received a minimum of 2 courses of salvage regimens prior to ASCT, while 6 patients received front-line transplant. Disease status at transplant was: CR in 44 pts, PR in 20, active disease in 43. After a median follow-up of 2.4 years (range 1-16 years) post transplant, 32 pts died (26 for relapse and 6 for early or late toxicity without relapse). Overall survival (OS) at 3 and 10 years was 69.9% and 57%, respectively; the incidence of relapse was 45% and 50%, respectively. According to the disease status at transplant, the probability of survival at 10 years was 75% for patients in CR or PR and 33% for patients with active disease. The incidence of relapse was 37% and 71.2% respectively. In the whole group, four patients developed a second cancer: three of them had relapsed after ASCT. The cumulative actuarial probability of a second cancer was 2.3% at 5 years: it was nil for patients who did not relapse after transplant and 11.1% for patients who needed additional chemotherapy for relapse (P 0.03).

Conclusions: a) Disease status at transplant had a significant impact on relapse-free survival; b) A significantly higher risk of second cancer was observed among patients relapsing after ASCT.

564 PREVENTION OF TREATMENT-RELATED OVARIAN DAMAGE IN YOUNG WOMEN WITH HODGKIN'S LYMPHOMA (HL) BY GONADOTROPIN-RELEASING HORMONE ANALOGUE (GnRHA)

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Introduction: Most patients (pts) with HL can be cured since many years. Consequently, the follow-up of HL survivors has shown the development of treatment-related (TR) late adverse effects. Particularly, TR ovarian failure causes amenorrhea and infertility in young women, depending on the type and intensity of treatment. So, oral contraceptive, GnRHa and oophorectomy are used for the prevention of ovarian damage.

Pts and Methods: From 1994 to 2006, we treated 62 consecutive women with a median age of 27 years (14-45). 47 pts were in clinical stage (CS) I-II, 15 in CS III-IV; 26 pts had B symptoms. Pts received ABVD (20), ABVD+Radiotherapy (RT) (25), BEACOPP (1), BEACOPP+RT (1), VBM+RT (2), COPEBVCAD (3), COPEBVCAD+RT (3), ABVD+IGEV (1), ABVD+IGEV+ Peripheral blood stem cell autografting (PBSCA) (5), ABVD + COPEBVCAD + PBSCA (1). 1/31 irradiated pts received subdiaphragmatic RT. To avoid the gonadotoxicity, all pts received Triptorelin 3.75 mg monthly until treatment conclusion. A questionnaire has been used to evaluate the menstrual status and pregnancy before and after therapy.

Results: All pts are alive and HL-free. Before the treatment, all pts had normal menses; one showed infertility. After a minimum of 6 months from the end of the therapy, 50 (81%) pts reported regular menses, 4 (6%) pts irregularity of the menstrual cycle and 8 (13%) pts became menopausal. The last 8 pts received ABVD+IGEV+PBSCA (5), ABVD+COPEBVCAD+PBSCA (1), ABVD+IGEV (1) and ABVD (1, a 45 years old woman). 13 pts (treated with ABVD or BEACOPP or VBM) have a pregnancy wish and conceived; 12 healthy babies were delivered and 2 pregnancies are ongoing.

Conclusions: In our experience, GnRHa is able to prevent TR ovarian failure and infertility in pts receiving a single line of polichemotherapy + supradiaphragmatic RT. On the contrary, it is ineffective during sequential intensive courses of polichemotherapy, specially if associated to PBSCA. In these pts new approaches are needed. In our opinion, cryopreservation of ovarian tissue before the treatment with its later reimplantation should be one of the most promising modalities. So, first of all, the challenge is to identify the pts surely at risk of infertility.

565 PREVIOUS FLUDARABINE TREATMENT IS A STRONG PREDICTOR FOR LONG-TERM CYTOPENIA IN NON-HODGKIN LYMPHOMA (NHL) PATIENTS TREATED WITH Y-90 IBRIDTOMAB TIUXETAN

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Background: The impact on myelosuppression of previous Fludarabine-containing treatment in patients treated with Zevalin is not well-defined.

Methods: Hematologic toxicity in patients with recurring NHL treated with Zevalin (0.4 mCi/kg) was compared according to +/- Fludarabine-containing regimens prior to Zevalin.

Results: Hematological toxicity are shown in the table.

	Fludarabine median (range)	Non-Fludarabine median (range)	Significance
Patients	6	20	
Age	53 (48-64)	61 (49-82)	P < 0.05
N regimens prior to Zevalin	2.6 (2-4)	2.3 (1-5)	not significant
Anaemia (weeks)	0.4 (0-2)	0.0 (0)	not significant
Thrombocytopenia (weeks)	16.8 (0-67)	1.1 (0-6)	P < 0.01
Neutropenia (week)	12.5 (0-67)	1.6 (0-14)	P < 0.05

Grade 3-4 hematological toxicity: haemoglobin < 6.5 g/dl, platelets < 50000 platelets, absolute neutrophil count < 1000 cells/ μ l.

Conclusions: Patients with relapsed NHL treated with Fludarabine prior to Zevalin had significantly longer median duration of neutropenia and thrombocytopenia, than a moderately older group of NHL patients not previously treated with Fludarabine.

566 HIGH INCIDENCE OF INFECTIONS ASSOCIATED WITH THE USE OF MAINTENANCE RITUXIMAB MONOTHERAPY IN NON-HODGKIN'S LYMPHOMA (NHL)

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Introduction: Rituximab is a chimeric monoclonal antibody that targets CD20, a surface antigen found on all B lymphocytes. It is used as maintenance treatment for relapsed low-grade NHL, improving disease-free and overall survival. Low infections rates with rituximab monotherapy have previously been reported.

Methods: 32 patients with NHL, treated with a minimum of 12 months of maintenance rituximab monotherapy at Barwon Health from 1st January 2003 to 30th September 2007, were identified. The incidence and sites of infection while receiving maintenance rituximab were recorded, as was histology, date of diagnosis, duration of rituximab treatment, age, gender, prior treatments, and frequency and severity of hypogammaglobulinaemia.

Results: 23 infections were observed in 16 of 32 patients (50%). Commonest sites of infection were respiratory tract (14), skin (4) and urinary tract (3). 6 of the 23 infections led to hospitalisation. Compared with those who did not, patients developing infections were older (average 73 years versus 65), had a longer average duration of disease (94 months versus 56 months), a longer average duration of rituximab treatment (32 months versus 16 months), were more likely to have hypogammaglobulinaemia (16 of 16 versus 12 of 16), and had greater average decreases in serum IgG (12% versus 4%) and IgA (20% versus 9%) levels during treatment. 6 of 8 patients previously treated with a fludarabine-based regimen developed infections, whereas only 7 of 13 who had received an anthracycline-based regimen did so. There was little difference in the average number of previous treatments (1.9 versus 1.7) and infection rates were similar for both sexes (7 of 12 males, 9 of 20 females).

Conclusion: The observed infection rate with rituximab maintenance treatment was higher than previously reported. Risk factors for infections included longer duration of disease and of rituximab treatment, age, previous fludarabine-based treatment, and hypogammaglobulinaemia.

567 RITUXIMAB FAST INFUSION TOLERANCE

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Introduction: Rituximab was a big step forward for treating patients with B-cell lymphoproliferative syndrome. Due to the toxicity of the infusion rate, guidelines recommend to start with a rate of 50 mg/hour and increase the rate to a maximum of 400 mg/hour. There have recently been several studies published about fast infusion; our objective is to evaluate Rituximab fast infusion reactions and the ability to predict tolerance in the subsequent cycles depending on the maximum rate achieved in the initial infusion.

Methods and Methods: We studied B- lymphoproliferative CD20+ disorders (except CLL) that were going to be treated with chemotherapy and Rituximab. Patients with bulky disease or big tumour mass were treated with a first chemotherapy cycle. We used standard infusion guidelines for the initial infusion. If the patient tolerated initial infusion to a maximum of 400 mg/hour, we started at that maximum rate in subsequent infusions. Those patients who did not tolerate initial infusion were excluded from the study. Pre-treatment with acetaminophen and diphenhydramine was administered in all patients.

Results: 78 patients were studied with a total of 403 Rituximab infusions. 50 were men and 28 women, with a median age of 63 years old (range: 18-82). 43% were diffuse large B-cell non-Hodgkin's lymphoma (NHL), 15% Mantle Cell Lymphoma, 2% Small-B-Cell Lymphocytic Lymphoma, 34% Follicular NHL, 2% Burkitt lymphoma, 2% Marginalzone lymphoma, 2% Waldstrom Macroglobulinemia. Two patients had a reaction to initial infusion, one had a bronchospasm and the second one had abdominal pain. For these patients we used regular infusion guidelines in the subsequent infusions. The rest of the patients received Rituximab at a 400 mg/ hour infusion rate from start to finish without reactions.

Conclusions: In patients that tolerate a 400 mg/hour infusion rate, subsequent infusions can be administered from the start at 400 mg/hour. Quality of life improved in these patients due to the reduced time period at the day clinic, also reducing the use of resources and time by an average of 90 minutes.

568 RITUXIMAB-RELATED URticARIAL REACTION IN CUTANEOUS B-CELL LYMPHOMA

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Introduction: Few cases of rituximab-related urticarial reaction have been reported in patient treated for B-cell lymphoma, especially cutaneous lymphoma. This

phenomenon may be related to the killing of tumoral CD20 B-cells in the site of the tumor.

Material and Methods: We report another case of urticarial reaction during rituximab infusion in a patient with cutaneous lymphoma despite premedication with antihistamine and steroids.

Results: A 43-year-old man was referred to our hospital because of unusual erythematous skin patches involving the dorsal right infra-axillar regions. Biopsies confirmed the diagnosis of cutaneous follicular B-cell lymphoma. Complete evaluation did not reveal systemic disease. After an unsuccessful treatment with topical steroids, external radiotherapy was delivered with complete remission. However, a cutaneous relapse occurred two years later with thoracic and dorsal lesions. The patient was treated with 4 weekly intravenous infusions of 375 mg/m² of rituximab, the first infusion over a 6 hours period, and the 3 consecutives over 1 hour. One hour after the start of the first infusion and despite pre medication with diphenhydramine, acetaminophen and steroid, the patient developed an urticarial reaction at the site of tumours patches and excision scars. The patient could therefore complete the planned treatment with no side effects. Evaluation after the four cycles showed a complete remission status. The patient is still in complete remission with a 12 months follow-up.

Conclusions: To date, few cases of localized rituximab-related urticarial reactions have been described. These cases show urticarial lesions only localized on the tumor sites and occurring during the first infusion. The mechanism of these reactions remains unknown but may represent an indirect sign of anti-tumoral effects of rituximab on malignant CD20 B-cells. Of note, all three patients reported experienced a complete remission after rituximab monotherapy treatment. Thus in case of cutaneous B-cell lymphoma, in particular follicular subtype, the first infusion of rituximab can induce urticarial reaction located to the tumor sites, even in patients treated with antihistamine and steroids.

569 EFFICACY AND TOLERABILITY OF RITUXIMAB-BASED CHEMOTHERAPY IN CD20 POSITIVE NON-HODGKIN LYMPHOMA

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Background: Introduction of rituximab to the treatment of CD20-positive NHL became a cornerstone in the modern management of this entity. The purpose of this retrospective study was to evaluate the efficacy and tolerability of rituximab combined with chemotherapy, based on the FDA/EMA treatment approval in particular CD20-positive NHL.

Methods: Between 2002 and 2006 56 patients (34 women and 21 men), median age 51 years (range 18-72) with newly diagnosed B-cell NHL were treated in our department. 43 patients (76%) suffered from diffuse large B-cell lymphoma (DLBCL), 10 (18%) were diagnosed with follicular lymphoma, 3 (6%) had other indolent lymphoma histology. According to the IPI score 53.5% had low risk disease, 28.5% low-intermediate, 16% high- intermediate, 1 patient had high risk disease. In 51 patients rituximab was added to CHOP regimen and in 5 patients to COP regimen. The median number of rituximab doses was 6.

Results: Overall response rate (ORR) was 83.6% with complete regression (CR) rate 64%. Stable disease (SD) occurred in 4.1% of cases, and disease progression (PD) was observed in 11.6% of patients. In DLBCL patients CR was achieved in 27 (62.7%) patients, partial regression (PR) in 9 (20.9%) and SD in 2 (4.6%) patients. 5 patients had progression. With median follow-up of period 34 months 2-year progression-free and overall survivals were 75% and 81% respectively. In Cox proportional-hazards model only IPI >2 score had negative impact on overall survival (p=0.047). Toxicity was mild, the most common adverse events (grades 1-2) were neutropenia (7%), stomatitis (4.3%), peripheral neuropathy (4.3%), there were only 3 infectious complications and 2 cardiovascular incidents, no grade 4 toxicity was observed.

Conclusions: Rituximab-based chemotherapy is effective and well-tolerated treatment modality for CD20 positive non-Hodgkin lymphoma patients. However, patients with high-intermediate and high IPI score might not benefit enough from such treatment, and optimal therapy for these cases needs to be determined.

570 CARDIOVASCULAR STATUS IN THE SURVIVORS OF LYMPHOMA TREATED WITH DOXORUBICIN CONTAINING CHEMOTHERAPY

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Introduction: Risk of serious late cardiovascular complications after anthracyclines containing chemotherapy is notably higher compared to corresponding population. The aim of our study was to determine the occurrence of late doxorubicin cardiotoxicity and the cardiopulmonary performance status in the patients surviving more than 5 years.

Material and methods: 363 patients with Hodgkin's and non-Hodgkin's lymphomas were treated with doxorubicin (in CHOP and ABVD regimens) at our

department 1995-2000. 229 (63%) of them survived more than 5 years and 96 were consecutively included in our prospective study. 47 male, 49 female, median age 41 (23-79). The median follow-up was 6 years (5-10). Patients were examined by rest echocardiography before initial treatment, after its completion and at the minimum follow-up of 5 years. Dynamic stress echocardiography, cardiopulmonary exercise test, ECG and blood pressure Holter monitoring, variability of RR interval and laboratory tests of BNP were performed.

Results: Clinical doxorubicin induced cardiotoxicity was observed in 6% of pts (drop-off ejection fraction, EF<50%), subclinical cardiotoxicity in 31% in median cumulative dose of doxorubicin (CD DOX) 300 (50-880) mg/m². Diastolic dysfunction was detected in 38% patients. Decrease of EF significantly correlates with duration of follow-up. The risk factors for late cardiac toxicity in multivariate analysis were CD DOX ≥300mg/m², pre-existence of cardiovascular diseases and age >60 (for CD DOX p<0.05; age p<0.01; concomitant cardiovascular disease p<0.01, r=0.57 and p<0.02 for whole model). Additional treatment following the initial treatment is associated with higher risk only for finding of diastolic dysfunction (OR=2.37, p<0.05), but not for drop-off LVEF. Reduced cardiopulmonary performance was detected only in 15% of survivors and is significantly affected by age and diastolic impairment. Assays for the plasma BNP seems to be useful to diagnose late myocardial dysfunction using stadard cut-off value 29 pmol/l. The findings on heart rate variability examination, ambulatory blood pressure and ECG monitoring revealed a good correlation with the advanced age and with the presence of concomitant cardiovascular diseases. They do not reflect the late toxicity of anthracycline treatment in our study.

Conclusions: Our results demonstrate, that besides the standard assessment of left ventricular systolic function, also the diastolic function should be an integral part of echocardiographic examination and cardiac functions should be monitored long term in patients after anthracycline containing regimens.

571 CARDIOMYOPATHY IN PATIENTS TREATED FOR LYMPHOMAS BY ANTHRACYCLINE-CONTAINING CHEMOTHERAPY

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By means of echocardiography we have assessed 112 survivors over the period up to 30 years after primary therapy of lymphomas that were treated in Cancer Research Center of Russian Medical Academy of Science (CRC) between 1973 and 2003.

The schemas of chemotherapy containing anthracyclines were ABVD, BEACOPP, and CHOP.

The heart ultrasound investigation of our patients revealed decrease of median of left ventricle ejection fraction in mid-term and in late-term survivals.

Comparison of ejection fraction in groups of patients before, immediately after the course of treatment and more than 6 months after the treatment shows significant difference in its values [68.0 (54.2–82.8)%, 65.1 (48.9–75.1)%, 63.9 (25.6–80.7)% respectively, p=0.003] due to presence of patients with depressed left ventricle systolic function in group of late survivals.

It is of particular interest to note that severe impairment of left ventricular ejection fraction was found in patients with normal or small end diastolic volume and that no patients with ventricle dilation were detected. While index of end diastolic volume did not differ between groups, significant difference between them in values of index of end systolic volume [15.9 (9.6–31.9) ml/m², 16.2 (7.9–29.0) ml/m², 19.1 (6.8–56.3) ml/m² respectively, p=0.044] was identified. Besides, lymphoma survivors with previous anemia reveal statistically significant lower left ventricular myocardial mass index (LVMM), end diastolic volume index (IEDV) and stroke index (SI), and positive correlations between initial hemoglobin levels and LVMM (r=0.32, p=0.004), and IEDV (r=0.26, p=0.01), and SI (r=0.25, p=0.024). Initial hypoproteinemia in our patients was commonly associated with lower ejection fraction (p=0.01) and LVMM (p=0.04). This statistically significant correlation of echocardiography indices with initial hemoglobin level and total protein level before chemotherapy enables their use as predictors of heart failure in patients with lymphoproliferative disorders receiving antitumor therapy along with anthracycline antibiotics.

572 PROSPECTIVE EVALUATION OF EARLY DOXORUBICIN (DOX) CARDIOTOXICITY IN LYMPHOMA

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Introduction: Anthracycline (AC) cardiotoxicity (CTOX) is well recognised and dose limiting, but this drug class is likely to remain a crucial component of curative regimes for Non Hodgkin Lymphoma (NHL) and Hodgkin Lymphomas (HL). Although there are likely to be many common factors influencing CTOX in patients receiving AC, the effect may differ depending on tumour type, other co-administered drugs and pre-treatment host factors. The magnitude and incidence of CTOX has been extensively reported but few studies have prospectively studied cardiotoxicity in lymphoma patients.

Methods: between 2003 and 2007, 111 patients aged 16-89 without a history of prior AC exposure were enrolled at a single centre for prospective evaluation by two

dimensional echocardiography (EC) of CTOX before, during and within 9 months of completing DOX containing regimens. Standard definitions based on left ventricular ejection fraction (LVEF) were used to define CTOX.

Results: 8 patients were found to have pre-existing heart disease, 2 withdrew, 12 died, 1 developed atrial fibrillation and one had a myocardial infarct. 65 NHL and 24 HD were evaluable for cardiac specific follow up. 13 NHL and no HL patients developed functional CTOX. A number of pre treatment variables, early diastolic change and total DOX dose were analysed as possible predictive factors for early CTOX. Age, lymphoma type, diastolic dysfunction and Tei index were found to be significant on univariate analysis. However, only pre-treatment haemoglobin and albumin levels were significant on multivariate analysis.

Conclusions: 1) Prospective evaluation identifies pre-and intra treatment cardiac disease in an unselected cohort of lymphoma patients. 2) Significant numbers of AC treated patients develop CTOX at relatively low DOX doses. Further follow up will be needed to assess long term implications. 3) Although various factors predictive of early CTOX were identified, these are unlikely to be clinically useful in treatment planning at present. They may have relevance to the aetiology and prevention of CTOX. 4) Early EC changes may serve as a surrogate for long term clinically significant CTOX and as a trigger to consider cardiac specific monitoring and intervention during treatment.

573 HEMATOLOGICAL TOXICITY OF IBRITUMOMAB (ZEVALIN) USED AS A CONSOLIDATION STRATEGY

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Introduction: Although Zevalin allows to achieve a response even in heavily pretreated FL patients, long lasting PFS are observed almost entirely in those achieving CR. While escalating radioimmunotherapy (RIT) is not possible (dose limiting hematological toxicity), using Zevalin as a consolidation strategy, after pretreatment to reduce tumor load looks promising.

Material and methods: Hematological toxicity of Zevalin used as a consolidation strategy in MCL (n=45) was assessed and compared with RIT toxicity in relapsed FL (n=21). Bone marrow involvement was comparable in the two groups, with CD 20

infiltration below 15%. In MCL RIT was a consolidation of the first or 2 nd treatment line, while most of FL patients were heavily pretreated (after failing 2-6 previous regimens). In both groups Zevalin (0.3 or 0.4 mCi/Kg, based on initial platelet count; max dose=32 mCi) was proceeded by 2 doses of Rituximab (250 mg/m² on days 1 and 8).

Results: Hematological toxicity of RIT in FL patients, was similar to described in US registration trials: leucopenia (WBC <2000/ul) and thrombocytopenia (Platelets <50 000/ ul) began 3-4 weeks after procedure and lasted for 2.9 and 3.7 weeks respectively (Tab. 1). It was not influenced by Fludarabine based regimens, used in previous treatment lines. The length of cytopaenia was significantly prolonged in patients consolidated with RIT after FC-R and especially FCM-R (p<0.05). More patients required RBC and Platelet transfusions (50 % vs 15%), there were more infections requiring hospital admission (43 vs 14.3%). One procedure related mortality was reported (hemorrhagic stroke at day +80). Relatively low toxicity RIT consolidation after CHOP-R was reported in ECOG study (Smith et al., ASH 2007). Our data suggest similar results, however there are not enough patients for statistical analysis.

Conclusions: Good clinical efficiency of RIT consolidation strategy has a considerable hematological toxicity, especially if used after fludarabine based regimens.

Proceeding chemotherapy	WBCs < 2000/uL (weeks)	PLTs <50 000/ul (weeks)	Pts with Infections	Pts with RBCs transfusions	Pts with PLTs transfusions	Patients on G-CSF
None (N=21)	2,9 (range 0-15)	3,7 (range 0-12)	14,3 (%)	15 (%)	14,3 (%)	23,8 (%)
CHOP-R (N=5)	2,0 (range 0-10)	1,0 (range 0-5)	20 (%)	20 (%)	0 (%)	0 (%)
FC - R (N=10)	8,4 (range 0-17)	7,2 (range 0-14)	20 (%)	30 (%)	20 (%)	10 (%)
FCM -R (N=30)	6,3 (range 3-20)	7,2 (range 2-24)	43,3 (%)	50 (%)	50 (%)	23,3 (%)