

Material and Methods: Retrospective review of 295 stage I-II DLBCL patients (pts) treated with curative intent between 2002 and 2008. All pts had CMT and received RT at our hospital. Primary CNS lymphomas were excluded. Median age was 61, with M:F ratio 1.14. Ann Arbor stages were IA – 48%, IIA – 41%, I-IIB – 11%. Extranodal involvement was present in 66% (IE: 34%, IIE: 32%), and bulky disease (≥ 10 cm) in 22%. Chemotherapy included: cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP, in 32%) and R-CHOP (65%), median 6 cycles (22% had 3 cycles). Median involved-field RT dose was 35 Gy, with 97% receiving ≥ 30 Gy. The median follow up was 4.2 yrs (6.8 yrs for CHOP-treated, 3.8 yrs for R-CHOP). In pts with disease progression or relapse, the site(s) of failure were documented to determine if it occurred in the RT field (local), at field margin or out-of-field (adjacent nodal region, or distant).

Results: Response was evaluable in 292 pts, with CR/CRu in 282 (96.6%) and \leq PR in 10 (3.4%). To date, 30 patients relapsed. Failure sites for relapsed pts were: 2 local, 1 marginal, 23 distant, and 4 were both local and distant. No failures were seen in an adjacent nodal region. The cumulative 5-yr local disease failure rate was 6%, and was higher in the CHOP vs. R-CHOP patients – 12% and 2% respectively ($p = 0.001$). Of the 2 isolated local failures, 1 had suboptimal therapy (3 CVP follow by RT 28 Gy). The 5-yr distant disease failure rate was 12% (for CHOP: 14%, vs. R-CHOP: 10%, $p = 0.28$). To date, 40 deaths occurred (17 due to disease, 23 other causes) with actuarial 5-yr clinical outcomes: overall survival – 87% (95% CL, 82–91%), cause-specific survival – 94% (95% CL, 90–96%).

Conclusions: Modern CMT for stage I-II DLBCL has excellent clinical outcomes including very high local control rates. Adjacent nodal region failure is not a clinical problem for involved-field RT covering initial disease only.

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POSTER

The Role of Palliative Radiotherapy in Patients With Myeloma Bone Disease in the Era of the Novel Agents

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Background: The introduction of the novel agents Bortezomib, Thalidomide and Lenalidomide changed the philosophy of the treatment in multiple myeloma (MM) and the fate of the patients.

Aim: To analyze the application of palliative radiotherapy in incidence, outcome and time to first skeletal related event after radiation in patients with myeloma bone disease (MBD) receiving conventional chemotherapy (CC) or Bortezomib+Dexamethasone (VD) regimen.

Patients and Methods: For the period 1995–2010, 341 patients with MM were studied, m/f ratio 1.2/1, mean age 60.6 (32–83). The staging systems of Durie et Salmon and ISS were used. MBD was graded according to the Merilini scale. VD was applied in 27 patients. Biphosphonates were administered by the general rules. No significant difference was found in the distribution in sex, age, clinical stage, grade of MBD, and major parameters of the disease between the two groups. Statistical analyses were performed by variative, correlative, alternative analyses, independent samples T-test, one-way ANOVA and Kaplan Meier test (SPSS v15).

Results: In the group on CC in 136 (43.3%) MBD grade II and in 25(8%) MBD grade III was found, 47(15.0%) had soft tissue formations. In the VD group 11(40.7%) had MBD grade II; 4(14.8%) had MBD grade III, plasmocytomas – 5(18.5%). 162 (51.6%) patients on CC and 16 (59.3%) on VD were irradiated. Pathological fractures were irradiated in 105 (77.8%) in the CC group and in 10 (90.9%) in VD, the severe skeletal destructions were irradiated in 24 (96.0%) vs 4 (100%), plasmocytomas in 37 (78.7%) vs 5 (100%) respectively. In 134 (82.7%) of CC patients pain alleviation was achieved, in 92 (87.6%) the fractures were stabilized, in 30 (81.1%) a reduction of the soft tissue formations occurred. In VD group pain was alleviated in 13 (81.3%), fracture stabilization occurred in 8 (80.0%), and plasmocytoma reduction in 5 (100.0%). Median time to reappearance of bone pain after radiotherapy in the CC group was 10 months (9–12) and to a new fracture 13 months (12–15). The median time to a skeletal related event for the VD group is not reached yet.

Conclusions: In the era of the new agents palliative radiotherapy is still an effective method in the treatment of MBD: it significantly alleviates pain, results in stabilization of the pathological fractures, reduces the size of the soft tissue formations and improves the quality of life of patients, not compromising further antitumour treatment.

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POSTER

Cardiac Effects After Low-dose Whole-heart Radiotherapy Following Doxorubicin-based Chemotherapy in Hodgkin's Lymphoma

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Hodgkin's lymphoma (HL) may present with extensive pericardial disease or cardiophrenic lymphadenopathy. Partial or poor response to first-line chemotherapy (CT) becomes a case for a whole cardiac radiotherapy (RT) with increased risk of cumulative CT-RT cardiotoxicity.

Using echocardiography we assessed the left ventricular function before starting CT for Hodgkin's lymphoma and after the end of treatment in total 152 patients (pts). Since 2000, in a prospective MRRC study HL patients stages II to IV were treated with 4–6 courses of BEACOPP-21 or ABVD followed by 1–2 COPP in order to reduce doxorubicin toxicity before consolidation RT. All patients received ⁶⁰Cobalt mediastinal irradiation to 20–22 Gy. Fifty eight patients of Gr. 1 presented with pericardial effusion and therefore received low-dose (10–17 Gy, median 14 Gy) whole cardiac RT in the course of mediastinal (16 pts) or wide-field irradiation (42 pts) as one of the two daily fractions delivered in accelerated hyperfractionated regimen (AHFX). In patients of the two control groups cardiac apex was shielded. The patients with residual mass after CT (Gr.2, n=45) received mediastinal irradiation in AHFX regimen, those with complete response (Gr.3, n=49) received RT in conventional fractionation once a day. Groups did not differ by doxorubicin dose (100–300 mg/m², median 150) and age at examination (20–57 years, median 32 years). Before CT, mean left ventricular ejection fraction (LVEF) was 64%; a systolic dysfunction (LVEF <60% or >72%) was more pronounced in Gr.1 (49% pts VS 27% pts in Gr.2 and Gr.3, $p = 0.03$).

After the combined-treatment program and after a median follow-up of 60 months, mean values of LVEF were, respectively, 62% (range, 50% to 75%), 63% (range, 54% to 70%) and 62% (range, 54% to 76%). LVEF below 55% was recorded in 7%, 4% and 13% pts, respectively, but none of the patients exhibited clinical signs of heart failure. Rest EF was correlated negatively with cumulative doxorubicin dose (Gr.1, $r = -0.83$, $P = 0.02$; Gr.2, $r = -0.97$, $P = 0.03$) and age (Gr.3, $r = -0.50$, $P = 0.017$). In patients aged ≥ 40 years, EF was correlated with the time from RT (Gr.1, $r = 0.56$, $P = 0.193$; Gr.3, $r = 0.75$, $P = 0.011$). Response to exercise testing with an increment of EF >5% was observed in 50%, 60% and 62% pts, respectively.

Our study suggested that low-dose irradiation of whole heart for extensive pericardial disease did not impaired significantly cardiac function during first decade after doxorubicin-based chemotherapy as compared with partial irradiation of heart. Further observation is necessary.

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POSTER

Impact of DeVIC as Chemotherapeutic Agent for Concurrent Chemoradiotherapy for Nasal NK/T-cell Lymphoma

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Background: Extranodal natural killer (NK)/T-cell lymphoma (NKTCL), nasal type, is a rare aggressive lymphoma with poor prognosis. This is an Epstein-Barr virus-associated lymphoma and the lymphoma cells expressed P glycoprotein, resulting in tumour multidrug resistance (MDR). Reported 5-year overall survival for patients with localized nasal NKTCL treated with CHOP is lower than 50%. DeVIC (dexamethasone, etoposide, ifosfamide and carboplatin) chemotherapy was designed as a salvage chemotherapeutic regimen for aggressive lymphoma comprised of MDR-unrelated agents and etoposide, which is thought to be effective against nasal NKTCL. We are now on the way to do an experimental chemoradiotherapy (CRT) using DeVIC as concurrent chemotherapeutic agents for nasal NKTCL. The aim of this study is to look at the initial outcome of this treatment to evaluate its effectiveness and feasibility.

Material and Methods: Six patients (range, 29 to 82; median, 68 years) were treated with CRT using DeVIC chemotherapy between April 2004 and February 2010. Median follow-up was 56 months (range, 11–80). Clinical features of these 6 patients were as follows: male:female = 4:2, 1E:2E=5:1, B symptom present = 0, elevated serum lactate dehydrogenase = 3, PS0:PS1 = 3:3, and IPI score low:low-intermediate = 3:3. All patients were given 3 to 6 cycles of full dose DeVIC regimen. The drug doses and administration schedule were as follows: dexamethasone, 40 mg/d on days 1 to 3, etoposide, 100 mg/m² on days 1 to 3, ifosfamide, 1.5 mg/m² on days 1 to 3, and carboplatin, 300 mg/m² on day 1. Basically the chemotherapy was given concurrently with radiotherapy (RT), and was

planned to repeat every 3 weeks. RT was performed using 4-MV X-ray, and the prescription dose was 46–50 Gy/23–25 fx. (median, 50 Gy) Clinical target volume included gross tumour volume and the entire nasal cavity and the ipsilateral paranasal sinus. After treatment, all patients were followed at our hospital.

Result: A complete remission was achieved in 5 patients (83%) at one month after treatment. Both the 5-year overall survival rate and disease-free survival rate were 100%. No severe adverse effect (grade 3?) have been found so far.

Conclusions: The initial results of the present experimental CRT with DeVIC for this aggressive lymphoma was absolutely excellent. This is encouraging and deserves a further study for concurrent CRT with 50 Gy/25fx. and 3 cycles of DeVIC comprised of non-MDR agents and etoposide for nasal NKTL.

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POSTER

Palliative Splenic Irradiation (PSI) in Haematologic Malignancies (HM)

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Background: Splenomegaly is a common complication in HM often associated with hypersplenism, and may cause pain, epigastric discomfort and variable systemic effects due to cytopenias. We retrospectively evaluated PRTS in terms of symptomatic relief in patients with HM.

Patients and Methods: In 1993–2006, 32 patients with HM (median age – 57) received PSI. Twenty one patients (66%) were diagnosed with myeloproliferative disorder (MPD), 5 patients (16%) had malignant lymphoma (ML), 5 patients (16%) had chronic lymphocytic leukemia (CLL), and 1 patient (3%) had hairy cell leukemia. Splenomegaly was accompanied by pain in 26 patients (81%), anemia in 20 patients (63%), thrombocytopenia in 17 patients (52%) and fever 3 patients (9%). Radiation therapy to entire spleen was delivered by 2 parallel opposed fields using 0.5 daily fractions given 5 days per week up to 6–10 Gy total dose. Survival was analyzed employing Kaplan–Meier method.

Results: PSI resulted in splenic size reduction in 85% of patients, improvement of anemia in 94% of patients and improvement of thrombocytopenia in 69% of patients. The median survival (MS) of pts with MPD, CLL and ML was 45, 10 and 5 months respectively. The MS of pts responders versus non responders was 55 and 16 months respectively (hazard ratio 0.17; $p = 0.03$; confidence interval 0.035–0.84).

Conclusion: In our hands, low dose PRTS provided effective palliation for patients with HM.

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POSTER

Acute Lymphoblastic Leukemia in the Adolescent and Young Adults: a Single Center Experience in Russia

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Background: Adolescents and young adults (AYA) with acute lymphoblastic leukemia (ALL) constitute a distinct population from children and older adults. Based on patterns of referral, they may be treated by either pediatric or adult hematologists. As a group, AYA with ALL have a worse overall survival (OS) and event-free survival (EFS) compared to that achieved by younger children. Original pediatric protocols ALL-MB 91 and 2002 have shown high efficiency of treatment of children in Russia. As a hypothesis we have assumed that outcomes for AYAs treated at adult and pediatric institutions will be equivalent when using therapy based on that used in pediatric cooperative group protocols.

The purpose of the study was to assess the efficacy and toxicity pediatric protocols ALL-MB 91 and 2002 for adolescents and AYA with ALL.

Materials and Methods: Enrollment on the study began in December 1997. Inclusion of patients (pts) in protocol ALL-BFM 90 ($n = 43$) was completed in September 2005 and ALL-MB 91/2002 – March 2008 ($n = 34$). In protocols ALL-MB 91/2002 the pts receive four drug induction with dexametazone 6 mg/m² daily for 36 days, daunorubicin 45 mg/m² for 2 doses, vincristine 2 mg weekly for 5 doses and intrathecal (IT) cytarabine and IT methotrexate and IT prednisolone weekly for 5 doses. Consolidation therapy included L-asparaginase in a constant dose of 10000 ME/m² weekly for 18 doses and 6-merkaptopurine 50 mg/m² (100%) daily and methotrexate 30 mg/m² (100%) weekly with weekly doses adjusted according to white blood cell count. Central nervous system (CNS) irradiation is performed for pts with CNS involvement at diagnosis and for patients with T-cell ALL and a high presenting white blood cell count.

Traditional maintenance was carried out up to 24 months. The protocol ALL-BFM 90 called for the purpose of comparison as an effective standard therapy.

Results: 78 ($m = 8$, $f = 30$) pts have been enrolled. 77 pts are valuable (1 withdrew on day 1 of therapy). The median age is 19.3 years (range 15–35). 37 (86%) pts are in complete remission (CR) on the protocol ALL-BFM 90 vs. 29 (88%) pts – ALL-MB 91/2002. Respectively 3 (7%) and 3 (9%) pts died in the induction. 3 (7%) and 1 (3%) pts is refractory to therapy. 5 (12%) and 1 (3%) pts died in CR from significant toxicities. Respectively 9 (21%) and 3 (9%) pts relapsed. 4 (33%) pts have CNS relapse, and 6 (50%) have bone marrow relapse. 6-years event free survival (6 y-EFS) has 54 vs. 77% (median of observation 5.7 years, $p > 0.05$), and 6-years overall survival (6 y-OS) has 65 vs. 82% ($p > 0.05$) respectively. Myelosuppression toxicities of ALL-MB 91/2002 protocols have less significant compared with the ALL-BFM 90. In postremission period the most frequent significant toxicities are neutropenia Grade 4 (21 vs. 66%, $p < 0.05$), and thrombocytopenia Grade 4 (0 vs. 62%, $p < 0.05$), and infectious Grade 3–4 (32 vs. 55%, $p > 0.05$).

Conclusions: Protocols ALL-MB 91/2002 is effective therapeutic regimes for ALL. Further studies with higher power are needed to determine if this treatment regimen offers an advantage to AYA patients with ALL.

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POSTER

G-CSF Administration in First Line Chemotherapy With ABVD for Hodgkin's Lymphoma in Adults

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Background: Hodgkin's lymphoma is a hematological malignancy originating from B lymphocytes, characterized by the presence of Reed-Sternberg cells amongst other reactive cells. Recent advances in treatment have allowed, even in advanced stages, an overall survival of up to 89% in 5 years. ABVD (doxorubicin, bleomycin, vinblastine and dacarbazine) is the most widely used chemotherapeutic regimen, also associated with significant pulmonary, cardiac and hematologic toxicity. Neutropenia, one of its most common adverse effects, may lead to dose-density alterations, possibly worsening long-term results. Our objective was to verify the role of G-CSF administration in the maintenance of ABVD regimen dose-density, in first-line treatment of Hodgkin Lymphoma in adults.

Material and Methods: We conducted a retrospective cohort of patients who had histologic diagnosis of Hodgkin's lymphoma confirmed by our department of Pathology, from 2004 to 2009 ($n = 272$). After application of admission criteria, 133 individuals were included. The patients were grouped according to prophylactic administration of G-CSF, which varied consonant different opinions of the doctors that integrated the Service, as there were no guidelines for this intent in use at the time of this Study. Statistical analysis was performed using SPSS version 18.0.2 program (SPSS Inc. ©, 2001, Chicago – IL, www.spss.com).

Results: We analyzed 1311 cycles of chemotherapy, administered for 133 patients, with a median of 12 cycles per patient [1;16]. There was a slight male predominance ($n = 67$), with a median age of 33 years [16;73] and no significant difference between sexes. Although associated with higher neutrophil counts in subsequent cycles ($p = 0.035$), administration of G-CSF resulted in no reduction in the frequency of treatment delays ($p = 0.510$). Overall toxicity was acceptable, with 4 episodes of grade 3–4 adverse events.

Conclusion: Administration of G-CSF didn't affect the dose-density of the ABVD regimen for first line treatment in Hodgkin Lymphoma in the studied patient sample, in spite of altering the neutrophils count. Hodgkin's lymphoma is probably a unique entity in which it is possible to maintain dose-density of chemotherapy without using hematopoietic stimulating factors, even in those patients who have neutropenia at the beginning of each cycle.

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POSTER

Alemtuzumab-based Conditioning of Allogeneic Stem Cell Transplantation – a Retrospective Analysis of a Single Center

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Background: Alemtuzumab-based conditioning of allogeneic stem cell transplantation (alloSCT) is used to lower the incidence of graft-versus-host disease (GVHD) in selected high risk patients. It is associated with high rate of mixed donor chimerism (MDC) and in some series with increased