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SELECTIVE ANTI-LEUKEMIC POTENTIAL OF HLA-INCOMPATIBLE BONE MARROW TRANSPLANTS

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We have shown that addition of G-CSF-mobilized peripheral blood progenitor cells to the marrow inoculum allows engrafment of T cell-depleted, haplo-identical marrow transplants for acute leukemia. Here, we report the post-grafting emergence of a large, donor-type $CD3^+/CD8^+$ T cell receptor ($T\zeta R$)-$\alpha\beta^+$ cell population, barely detectable in normal subjects, that expresses 58kD, "p58", inhibitory NK receptors for HLA-C locus alleles. Analysis of >900 clones revealed that 40% to 80% of these T cells exhibit NK-like function, i.e. they lysed class I-negative targets and were functionally blocked by class I alleles on target cells. MAb-mediated blocking of class I recognition by these cells induced lysis of HLA-protected, autologous targets. The class I-mediated inhibitory signaling through the NK receptors also blocked TcR/CD3-triggered cytotoxicity of these cells, indicating that their antigen-specific responses may be impaired. However, the NK-like function of these cells allows them to discriminate normal cells, protected from lysis, from leukemic cells which were lysed and may be targets for a graft-versus-leukemia effect.

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PRIMARY EXTRANODAL NON-HODGKIN LYMPHOMA OF HEAD AND NECK: THE EXPERIENCE IN TWENTY-EIGHT PATIENTS

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Our purpose is to report the experience in 28 primary extranodal non-Hodgkin lymphomas of head and neck during the period from March 1990 to February 1995. Extranodal involvements were tonsils in 13(46%), parotid in 3(11%), pharynx in 6(18%), nasal cavity in 2(8%), oral cavity in 3(11%), and paranasal sinus in 1(4%) patient. Histologic grading could not be identified in 2 patients, but fifteen patients(58%) were in intermediate and 11 patients(42%) were in low-grade. Distribution of stages in 26 patients were as following; 14(54%) in stage I, 9(35%) in stage II, 1(4%) in stage III, and 2(8%) in stage IV. Of the 22 patients treated, 14(64%) received both chemotherapy and radiotherapy, 7(32%) received only chemotherapy and 1(5%) received only radiotherapy. Half of the patients were given CNOP regimen and the rest were given various regimens i.e m-BACOD, BACOP, COP, and CHOP. Overall response rate was 90%(58% complete and 32% partial response) and median survival duration was 18 months(ranged from 6 to 59). Prominent toxicity was myelosuppression(22%).

Dominant features of our patients were common tonsil localization, frequent stage I existence, and high proportion of intermediate grade. The median survival duration was shorter than expected and not in accordance with high response rates.

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Salvage treatment of previously treated patients with advanced stage Hodgkin's disease with CCNU, etoposide and prednimustine (CEP) therapy

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Between 1984 and 1994, 85 patients (39 females and 46 males) with relapsed or resistant Hodgkin's disease were treated with CEP polychemotherapy. Their median age was 38,2 years. Most of the patients had advanced disease (stage III: 31 , stage IV: 35), 57 patients had B symptoms and 50 cases had bulky disease. An average of 30 months elapsed from the confirmation of the diagnose to the start of CEP therapy. Complete remission (CR) was achieved in 12 patients (40%), partial response (PR) in 34 patients (40%). The mean duration of remission was 67,3 months in CR and 11,8 months in PR. Thirty-nine patients (46%) did not respond to the therapy. Most frequent side effects were nausea, vomiting, myelosupression and alopecia. Treatment-related death did not occur. The authors consider CEP suitable for salvage chemotherapy of anvanced Hodgkin's disease.

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PULMONARY IMPAIRMENT IN LONG-SURVIVORS OF HODGKIN'S DISEASE (HD)

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Patients (pts) with HD can suffer from pulmonary toxicity after both chemotherapy (CT) (particularly after bleomycin) and radiotherapy (RT) (the mantle field involves mediastinum and lung apices). **Pts and methods:** Spirometry, carbon monoxide diffusion capacity (KCO), analyses of blood gases at rest and during exercise were performed in 27 pts (age: 27-59 yrs), 5 - 23,9 yrs (median: 13,1) after the end of therapy (mediastinal RT, 20-45 Gy: 23 pts, bleomycin: 16 pts). **Results:** Dyspnoea on exertion was reported in 8 pts. The mean values of the vital capacity (VC), residual volume/total lung capacity (RV/TLC) and KCO significantly deviated from the predicted normal values ($p = .003$, $p < .001$ and $p < .001$, respectively). VC values were < 60% in 4 pts. VC and RV/TLC seem to correlate with mediastinal bulky disease ($p = .14$), RT ($p = .13$), relapse of HD ($p = .12$) and length of follow-up ($p = .02$). KCO reduction was associated with bleomycin CT ($p = .054$) and was mild in all cases; it did not worsen with time ($p = .5$). No pt showed a significant decrease in SaO_2 during exercise.
Conclusions: A mild restrictive pulmonary defect is a common finding in long-survivors of HD. Pts irradiated for bulky mediastinal HD or treated for relapse have a higher risk of clinically significant respiratory impairment.

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A RETROSPECTIVE ANALYSIS OF 34 PATIENTS WITH PRIMARY GASTROINTESTINAL NON-HODGKIN'S LYMPHOMA.

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Many factors may influence the evolution and survival in primary gastrointestinal non-Hodgkin's lymphoma. To determine their importance, clinico-pathological and therapeutical aspects were analysed in 34 patients with primary gastrointestinal non-Hodgkin's lymphoma between Jan 1983 and Dec 1995. Diagnosis was performed with endoscopy-biopsy, surgery or both. Specimens were classified according to the Kiel classification and the MALT concept formulated by Isaacson. Staging was done according to the Ann Arbor staging system modified by Musshoff. Staging and follow-up included bone marrow biopsy, ultrasonography, chest-x-ray, computer tomography, regularly gastroscopy and in two cases lymphography. Therapy included surgery(SUR), chemotherapy(CT) and radiotherapy(XRT) in different combinations, but 19 patients of 34 received all of them. Survival was measured from initial diagnosis to either the end of follow-up or death. The average follow-up was 48 months (range 2-144). 29 of 34 patients(85.2%) obtained a CR, 2 patients(5.8%) achieved a PR. Progression was observed in only 1 patient. There have been 7 relapses: 4 of them died and 3 achieved a CR again. Patients in PR also expired. Overall survival ranged from 6 to 144 months(an average of 50.8) and disease-free survival from 3 to 131 months(an average of 46.9), respectively. The best overall and disease-free survivals were obtained with combination of SUR-CT-XRT followed by SUR-CT and CT-XRT. Outcome of stage IE was more favourable with no influence of histology. It is concluded, that SUR, CT and XRT applied together could prolong overall and disease-free survivals without increased risk of adverse reactions.

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AN APPROACH FOR EVALUATING THE COST-EFFECTIVENESS AND IMPACT ON QUALITY OF LIFE OF INPATIENT TREATMENT VERSUS OUTPATIENT TREATMENT DURING CONSOLIDATION CHEMOTHERAPY IN ELDERLY PATIENTS WITH ACUTE MYELOID LEUKEMIA (AML).

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In elderly patients with AML, the induction treatment requires 4-5 weeks of hospitalization. The aim of the phase III AML-13 trial of the EORTC Leukemia Group is to assess two types of consolidation chemotherapy in patients who reach complete remission after the induction cycle : 3 drugs during 7 days, using a classical continuous infusion, on an inpatient basis, or the same kind of drugs but delivered subcutaneously or orally, on an outpatient basis. In the second group, patients are hospitalized only in case of complications. The evaluation parameters are not only disease-free survival and overall survival, but also cost-effectiveness and quality of life.
The latter endpoints pose specific methodological challenges. We decided to use a diary to collect information concerning treatment compliance, side-effects of treatment and their impact on quality of life, and use of health care facilities. In addition information concerning resource utilisation during hospital treatment is being collected through the clinical Case Report Forms.
This communication aims to discuss the methodological approach to integrate economic and quality of life aspects in this large scale clinical trial.