These Topoisomerase-II inhibitors-type leukaemias display specific clinical and cytogenetic characteristics, such as short latency (median 18 months), monocytic phenotype and specific translocations. The potential relationship between dose, dose-intensity, pharmacological interactions with other drugs, and incidence of those SAL is yet undetermined.

Mat. and Methods: the data of 8 international phase III trials (7383 patients (pts), median follow-up 37–160 months) informative for anthracyclin-related SAL have been reviewed. The doses of anthracyclins used can be classified as low (Dox $\leq$ 50 mg/m^2/cy or 4-Epi $\leq$ 50–60 mg/m^2/cy, 1211 pts) or high (Dox $\geq$ 60 mg/m^2/cy or 4-Epi 100–120 mg/m^2/cy, 6172 pts).

Results: the observed anthracyclin-related SAL numbers regarding doses used are listed in the following table.

	Low doses Dox/4-Epi	High doses Dox/4-Epi
Total Nb Pts	11211	6172
Nb anthra-related SAL	1 (0.08%)	>26 (>0.4%)

These simplified data strongly suggest a dose-response relationship of anthracyclin-related leukemogenesis, which should be studied in a multifactorial model. Since early BC pts are more and more likely to receive high anthracyclin doses, a concerted and/or prospective effort is warranted to resolve these issues.

1339 POSTER

Survival analysis of an additional therapy with oral enzymes in patients with multiple myeloma

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The objective of this study was to assess existing data on patients with Multiple Myeloma (stages I–III) treated with different therapeutic regimens – Chemotherapy alone (VMCP/MOCCA, VAD) (CH) vs. Chemotherapy and additional treatment with oral enzymes (Wobe-Mugos®E, MUCOS Pharma, Geretsried, Germany) (OE). For this a retrolective cohort analysis in parallel groups of data of all patients diagnosed and treated in the Clinic of Haematology and Transfusion Medicine, Bratislava, from 1987 to 1997 (CH 99, OE 166 patients) was performed. Aim of this analysis was to investigate the effect of OE on survival. Primary efficacy parameter was the Kaplan-Meier-estimate of survival and the median survival time for both groups. Secondary parameters were response quality and response rate during the first year, duration of first remission, and the safety of a treatment with OE.

Both groups were comparable for their demographic data, and also for disease specific data. In the OE group for disease stage III median survival was 83 months compared to 47 months in the CH group (P logrank = 0.0014), and also for stages I–III survival time was longer in the OE group; adjusted sample (P logrank = 0.0003). In stage IIIA the resp. results were 88 vs. 49 months (P logrank = 0.0040), and for patients with renal insufficiency (stage IIIB) 66 vs. 37 months (P logrank = 0.1460). Multivariate Cox regression analyses confirmed these results. Response rates are higher and duration of remission is longer in the OE group. An early remission and a long duration of the first remission is an important prognostic factor for the survival of the patient.

Oral enzymes were well tolerated with 3.6% of the patients experiencing mild to moderate gastrointestinal symptoms.

The long term additional therapy with oral enzymes in patients with multiple myeloma receiving optimised chemotherapy regimens considerably prolongs survival. In our group of 265 patients median survival prolongation depended on disease stage, and on therapy with/without OE. Progression of disease stage increases the estimated mortality risk 5 to 6 fold, whereas OE decrease the estimated mortality risk by 50 to 60%.

1340 POSTER

Hodgkin's disease in the elderly – Less may be more

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Introduction: Patients with Hodgkin's disease (HD) older than 60 years have been treated at our institute with less aggressive approach in effort to minimise the side effects of chemotherapy and radiotherapy. The aim of the study was to compare our results with the data referred elsewhere and to establish the prognostic value of assessed factors.

Methods: From 1973 to 1993 there were 52 elderly (older than 60 years) patients with HD treated following Prague Cooperative Group protocol, which includes a relatively mild chemotherapy regimen (COPP) and/or limited field radiation techniques. Clinical stage, histological subtype, treatment modality, accomplishment of treatment, response to treatment, disease free survival (DFS), overall survival (OS) and tolerance of treatment were assessed using a retrospective analysis.

Results: Of the eligible 52 patients 30 (57.5%) achieved complete remission, 19 (36.5%) partial remission and 3 (6%) had a progressive disease during the treatment course. 5 year disease free survival was 48%. There were 2 independent prognostic factors for DFS and OS: Clinical stage (I, II vers. III, IV) ($p = 0.005$ and $p = 0.007$) and accomplishment of treatment ($p = 0.014$ and $p = 0.011$). There was no prognostic value of histological subtype. A marginally significant difference in DFS and OS is apparent between chemotherapy only (CT) and combined modality treatment (CMT) groups ($p = 0.005$ and $p = 0.06$). No significant difference was found between CT and radiotherapy only (RT) or CMT and RT treatment groups. However there is little covariation of clinical stage between CT or CMT and RT groups. The treatment was in general well tolerated with a very low rate of severe complications and no treatment related death.

Conclusions:

(1) With our less aggressive approach we achieved results comparable to those found in the literature while the tolerance of treatment was better compared to the studies employing more aggressive regimens.
(2) Our results indicate that less aggressive CHT approach may be compensated by addition of RT in favour of compliance in elderly patients with HD.

1341 POSTER

Bcl-6 gene alterations in non-Hodgkin's lymphomas

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Purpose: In the Western, rearrangements and point mutation (PM) of Bcl-6 gone can be identified in 20–40% and 70% of diffuse large-cell lymphomas (DLCLs). However, there are few reports concerning Bcl-6 gene alterations in Chinese non-Hodgkin's lymphoma (NHL) patients.

Methods: Lymph node samples obtained from 155 patients with NHLs (70 patients with DLCLs) were examined for the presence of gene rearrangements (GR) and PM in the Bcl-6 proto-oncogene using Southern blot analysis and single-strand conformation polymorphism followed by sequence analysis, the histopathologic classification with clinical outcome was then assessed.

Results: GR and PM in 155 NHL patients were 16.7% (n = 25) and 29.7% (n = 46) respectively. Meanwhile, in 70 DLCLs, Bcl-6 GR were identified in 13 (18.6%) and PM in 27 (38.6%). Bcl-6 PM occurred independently of Bcl-6 GR. All of Bcl-6 GR in NHLs were of the B-cell type, whereas 3 PM were derived from the T-cell lineage including a case of adult T-cell lymphoma. By Cox's proportional hazard model for risk factor, these two types of gene alterations in DLCLs or in all NHLs were not associated exclusively with extranodal sites and were not a prognostic predict.

Conclusion: The incidence of Bcl-6 alterations in DLCLs is lower in Taiwan than of in the Western. Clinically, these two types of gene alterations in DLCLs or in all NHLs did not appear to carry any prognostic significance.

1342 POSTER

Increase of the myelodisplastic syndrome (MDS) incedence in Chernobyl-contaminated regions of Belarus can be the first evidence of radiation-dependent leukaemogenesis

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In 1986–1992 Belarussian National Registry of Blood Disorders was created in our Institute. It covers 7 years before Chernobyl and all post Chernobyl period. During this years all cases of leukaemia and MDS were collected and analysed, and only from 1996 we were able to establish some disturbances, that seems to be radiation-dependent.

In the years 1996–1997 the increase of MDS among adults, who lives on the Chernobyl-contaminated territories of Belarus, has been found. The incidence for whole Belarus in 1996–1997 was 0.9 per 100.000 population and in contaminated Mogilev region it was 1.32 in 1996 and 3.04 per 100.000 population in 1997. The same picture was evidenced in other contaminated Gomel region: 1.53 in 1996 and 1.05 per 100.000 population in 1997. The FAB classification was introduced in Belarus since 1990 in

all haematological departments and it allowed to standardise diagnostic criteria of these disease. Therefore, this increase can not be attributed to the diagnostics errors. The fast transformation of MDS in acute leukaemia (AL) (during 8–16 months) in patients from this regions was also suspected. Our findings are similar to Japanese experience after A-bomb explosions, where the appearance of AL from MDS has been shown as a feature of radiation leukaemia. The increase of MDS could be the first sign of the radiation leukemogenesis in Belarus, that was most heavy contaminated after Chernobyl explosion.

1343 POSTER

Alterations in functional activity of thyroid parafollicular cells in the course of chemoradiotherapy of children with Hodgkin's disease

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Patients and Methods: 18 patients with II–IV stade Hodgkin's disease, their age ranging from 6 to 15 years (Me – 11 years). Were administered multiagent chemotherapy (MAC) (3 courses of ChVPP plus 3 courses of B – DOPA) and radiotherapy (RT) on the involved areas. The level of calcitonine (C) in blood plasma (N – 6–30 pg/ml) was measered employing the radioimmunologic method (ELSA – hCT kit, Franse) prior to the treatment, before each MAC course, before RT on neck area and after the completion of it.

Results: Before commencing of the treatment, C content in all the children was within the normal range (mean 16.9 ± 2.2 pg/ml, ranging from 10.3 to 2.5 pg/ml). No significant differences in the hormone level were found in patients with local and advanced disease (stade II – 13.7–2.4 pg/ml, stage IV – 12.5 ± 2.5 pg/ml). Over the first courses of MAC the changes in the hormone concentration were of wave – like nature: a sharp decrease after ChVPP regimen and then a rise to the initial level after B – DOPA. The data suggest that cytostatic agents included in ChVPP regiment or at least one of them produce a toxic effect on parafollicular cells (PFC) of the thyroid gland (TG). By MAC completion this pattern vanished, and gradual reduction of C down to 7.8 ± 0.3 pg/ml was observed (in 2 times). In 48% of the patients the C level below normal.

The changes in C content in blood plasma at neck irradiation depended on the dose delivered. After radiotherapy at a dose of 20 Gy the C level remained within the normal range (8.5 ± 0.91 pg/ml) and corresponded to its level at the time of MAC completion. An increase in the dose to 30 and 40 Gy resulted in the fall of the C level down to 6.8 ± 0.9 pg/ml and 4.2 + 0.03 pg/ml respectively, which is 1.2- and 1.8-fold lower that the C level at MAC completion. A month later after RT completion, the C level continued to decrease and lowered to 3.4 ± 0.05 pg/ml.

Conclusion: Both MAC and RT reduce functional activity PFC of TG, the degree of its inhibition depending on the radiation dose delivered.

1344 POSTER

Tailored-treatment for early stage Hodgkin's disease

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Purpose: To study the value of risk-adapted treatment in non-laparotomized patients (pts) with stage I–II Hodgkin's disease (HD).

Methods: From 1989 to 1996, 84 pts with clinically-staged supradiaphragmatic HD (median age 30 y, range 16–79 y; M/F = 38/46; clinical stage I/II = 16/68; LP/NS/MC histology = 6/54/23) were treated according to prognostic factors at presentation. Fifty-seven pts with one or more of the following features were defined as unfavorable group (UF): age > 50, "B" symptoms, Bulky disease (≥10 cm), ≥4 involved sites, "E" lesion, ESR > 50, LD histology. They received 6 cycles of MOPP/ABV hybrid chemotherapy (M/A) followed by mantle field irradiation (49 pts) or chemotherapy alone (8 pts). Twenty-three pts with no adverse features were defined as favorable group (F), and were treated by subtotal nodal irradiation (14 pts) or 4 cycles of M/A combined with mantle irradiation (9 pts). Four patients had a very favorable presentation (VF) of stage I high cervical disease, and received mantle irradiation alone.

Results: All pts achieved complete response. With a median follow-up of 43 m (range 7 to 109 m) there have been 6 relapses, 1 in the F group and 5 in the UF group. 5-y failure-free survival was 89% (VF/F/UF = 100/98/86%), and 5-y cause-specific survival was 98%, as only one patient died of disease. There were no toxic deaths and one patient developed mesothelioma as second primary tumor.

Conclusion: Prognostic-factor tailored treatment is an effective and well-tolerated therapy for early clinically- staged HD.

1345 POSTER

Relative dose intensity (RDI) related to international prognostic index (IPI) in chemosensitive elderly patients with aggressive non-hodgkin lymphoma (NHL). No benefits on disease-free survival (DFS) in high-risk patients

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Purpose: RDI and IPI are prognostic factors in elderly patients (pts) survival with aggressive NHL. To determinate the influence of RDI, we analyzed the risk of relapse, stratified on each group IPI, in chemosensitive pts treated with conventional CHOP.

Patients: Within a 14 years period, 261 elderly pts with NHL were treated with CHOP. Of this group, we analyze 165 pts with complete response (63%). Histology was intermediate-grade or immunoblastic, according WF. The median age was 67 years (R: 60–84), 97 (59%) female, elevated LDH level in 33 (20%), Ann Arbor stage I–II: 100 (61%) and III–IV: 65 (39%), performance status: 0–1 in 138 (84%) and >1 in 27 (16%). IPI subgroups low-risk (LR) 72 (44%), intermediate-low (IR) 61 (37%), and intermediate-high/high (HR) 32 (19%).

Results: The median RDI, according to Hryniuk method, achieved was 0.82, and the total-dose delivery was 94% planned chemotherapy. The median RDI were LR: 0.81; IR: 0.80; HR: 0.78, without significant difference. With median follow-up 41 months, relapsed occurred in 55 pts. The median DFS was 71 months (CI95%: 36–105), the 4-years PFS rates were in LR: 78%, IR: 50%, and HR: 20%, with significant differences (p = 0.001). When the results of the study were stratified in 2 groups: a) below median RDI, and b) over median RDI. We found that 4-years DFS in LR pts (67% vs. 80%, p = 0.04), and in IR pts (38% vs. 63%, p = 0.001), both with significant differences. In HR pts (22% vs. 22%) no significant differences.

Conclusions: This data shows, in elderly pts with NHL treated with CHOP, a DFS benefit in LR and IR pts who received RDI over median (>0.82). In HR pts, the RDI showed no impact in decreasing the risk of relapse. We suggest that, in these high-risk pts, the indication of full doses is controversial and should be evaluated.

1346 POSTER

Primary adult Western-type intestinal lymphoma (PAWIL) in immunocompetent patients: Prognostic factors, patterns of relapse and therapeutic outcome

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Purpose: To analyze prognostic factors, patterns of relapse and impact on survival and toxicity of surgical radicality in immunocompetent pts with PAWIL, focusing on diffuse large-cell subtype (DLCL).

Patients and Methods: 42 HIV – pts with PAWIL ('86–'98) were reviewed. Pts with Burkitt's (n = 2), indolent (n = 4), mantle-cell (n = 4), and peripheral T-cell (n = 1) lymphomas were excluded. Study group consisted of 31 pts with DLCL (20 M; 11 F): 21 had limited disease (stage I–II; LD) and 10 had advanced disease (stage IV; AD). Median age was 61 ys; 13 pts had ECOG-PS >2; 11 had B-symptoms; 11 had bulky disease; 19 had LDH ratio >1. Risk was low (IPI < 2) in 13 cases, intermediate (2–3) in 11 and high (4–5) in 7. Extranodal site was small bowel in 16 cases, colon-rectum in 11, both in 4. Pts with LD were treated with surgical resection followed by anthracycline-containing chemotherapy (CHT). Surgical resection was complete in 9 cases. Four pts with stage II2X did not complete the planned treatment because of fatal surgical complications. Pts with AD were treated with CHT alone.

Results: There were no cases of bleeding or perforation during CHT. Thirteen pts with LD achieved a CR; 4 had PD. Six pts with AD achieved a CR; 4 pts had PD. Four responders (2 with LD) relapsed. Sites of failure were abdomen (n = 9), central nervous system (CNS, n = 2) and skin (n = 1). Fourteen pts are alive (13 NED) with a median follow-up of 67 months (5-yr OS: 43%). Ten pts died of NHL and 7 of other cause (3 NED). Five-yr