fraction from treated and nuclei from untreated cells we demonstrated that K-562 nuclei underwent apoptotic DNA fragmentation when incubated with cytosolic extract from Gem treated SKW-3 cells. The resistance of K-562 cells can be explained by the expression of BCR-ABL which prevents the apoptotic cell death. Cytosinearabinoside (Ara C) and Gem showed similar cytotoxic profiles on K-562 cells after 48 h incubation (IC50 > 100 $\mu$M for Ara C and IC50 > 40 $\mu$M for Gem). The simultaneous exposure (72 h) of K-562 to Gem and hexadecylphosphocholine (HPC) caused synergistic cytotoxicity. 24 h incubation of K-562 cells with 50 $\mu$M Gem followed by 50 $\mu$M HPC for 24 h caused optimal growth inhibition. Gem was found to be effective against freshly isolated blasts from a patient with relapsed AML as measured by the MTT-assay. Taken together our data indicate that Gem can be of benefit for patients with leukemias not responding to standard protocols.

1356 PUBLICATION

## Cyclophosphamide, vincristine, epirubicin and prednisolone (ceop-100) in aggressive Non Hodgkin's lymphoma (ANHL)

S.E. Bavbek[1], M. Basaran[1], K. Uygun[1], S. Alici[1], E. Darendeliler[1], H. Onat[1]. [1]*Oncology Institute, University of Istanbul Istanbul, Turkey*

Combination chemotherapy (CT) with cyclophosphamide, adriamycin, vincristine and prednisolone (CHOP) remains the standard treatment for aNHL. We replaced adriamycin with the less cardiotoxic antracycline, epirubicin, in a phase II trial. Between 1993– 1998, 89 patients (pts) with intermediate/high grade NHL were accrued into the trial. CEOP-100 consisted of cyclophosphamide 750 mg/m$^2$, epirubicin 100 mg/m$^2$, vincristine 1.4 mg/m$^2$ on day 1, and prednisolone 100 mg days 1–5 every 21 days. Growth factors were used for secondary propylaxis of neutropenic fever. The treatment plan included 4 cycles of CT followed by involved-field radiotherapy in stage I–IIA disease; advanced disease received 6 cycles of CT and radiotherapy to bulky nodes. WHO criteria for toxicity was used. Pts who didnot achieve complete response (CR) after the first 3 cycles were given salvage CT and taken off the study. The median age was 45 (range: 15–76), the male/female ratio 58/31. There were 19 pts with stage I, 34 with stage II, 25 with stage III and 11 with stage IV disease; 32 pts (36%) had B symptoms. Histology (Working Formulation) was intermediate grade in 79 and high grade in 10 pts. 449 cycles of CT were evaluable for toxicity; 81% of the pts completed the treatment. Delay >1 week occurred in 16% of the pts; 10% needed dose modification. Toxicity (grade III–IV) was recorded as follows: neutropenia 10%, anemia 8%, thrombocytopenia 3%, mucositis 5% of the cycles. Five episodes of neutropenic fever developed. One patient died with acute heart failure. Of the 85 pts with measurable disease, 76% achieved CR, 18% had partial response (PR); one patient progressed during CT. Fourteen pts (22%) with initial CR relapsed; 12 relapsed during the first year and died after being refractory to salvage CT. One of the 2 pts who relapsed after one year responded to salvage CT and is still in second remission. Median follow-up is 34 months; median disease-free survival is 15.5 and median overall survival is 19 months. The cumulative 3-year and 5-year survival is 49% (95% CI: 43–55) and 44% (95% CI: 37–51) respectively. The CEOP-100 regimen is an active and tolerable outpatient regimen applicable in aNHL. Ongoing trials of regimens with better CR rates will hopefully result in better survival.

1357 PUBLICATION

## Prognostic factors in primary gastric non Hodgkin's lymphoma

M. Basaran[1], S.E. Bavbek[1], S. Alici[1], K. Uygun[1], O. Dogan[2], M. Agan[2], E. Darendeliler[1], H. Onat[1]. [1]*Oncology Institute, University of Istanbul, Istanbul;* [2]*Istanbul Medical Faculty, Pathology Department, Istanbul, Turkey*

Fifty-two patients (pts) with primary gastric nonHodgkin's lymphoma (PGNHL) treated and followed between 1991–1998 were retrospectively analysed for presentation characteristics and prognostic factors. Histology (Working Formulation), performance status (PS-WHO), stage (Ann Arbor), bulky disease (>6 cm.), beta-2-microglobulin (B2MG), lactic dehydrogenase (LDH), surgery, and response to chemotherapy (CT) were included in the prognostic analysis. Median age was 60 (range: 23–75); male/female ratio was 1:1. Twenty-one pts had a distinguishable MALT (mucosa-associated lymphoid tissue) based lymphoma; 8 had low grade and 13 had high grade MALT histology. The other 31 pts did not have MALT association; 2 had folicular mixed, 16 had diffuse large cell, 9 had diffuse mixed cell and 4 had diffuse immunoblastic histology. The stomach was diffusely involved in 81% of the pts. Seventeen pts had stage I, 15 had II, 14 had III and 6 had IV disease; 42% had B symptoms. Thirty-seven pts applied after surgery; 14 had subtotal and 23 had total gastrectomy. CT was given to 34 (92%) of the pts after surgery; a total of 49 pts received CT and 98% of the CT given was antracycline-based. Pts with stage I disease and high grade histology received adjuvant CT after surgery. Response was evaluated in 35 pts who had measurable disease after surgery of unresectable gastric lymphoma; complete response (CR) was achieved in 74%. With combined of surgery and CT, the CR rate was 79%. PS > 2, stage IV disease, and lack of CR to CT were the adverse prognostic factors for survival. Surgery, LDH and B2MG levels did not affect survival. Of all pts who underwent surgery, only two pts did not receive CT, one of them is alive without disease. The 5-year overall survival was 65%; the 5-year survival was 69% in pts with unresected advanced stage disease, 73% in pts with subtotal gastrectomy and 60% in pts with total gastrectomy. There was no significant difference in survival between pts with or without surgery, although pts without surgery had advanced, unresectable disease. We conclude that the role of surgery in primary gastric lymphoma is still unclear. It is evident that only a fraction of pts can be cured by surgery alone, and the role of surgery in addition to CT remains to be determined in randomized studies.

1358 PUBLICATION

## Aberrant immunoglobulin (IG) heavy chain glycosilation in igg multiple myeloma (MM)

I. Aurer[1], G. Lauc[2], D. Rendic[2], B. Labar[1]. [1]*University Hospital Center Rebro, Division of Hematology, Zagreb;* [2]*Faculty of Pharmacy and Biochemistry, Department of Biochemistry and Molecular Biology, Croatia, Croatia*

Glycosilation is the most important posttranslational modification of proteins in eukaryotic cells. While cells spend a large amount of energy on this process its importance in normal physiology and disease is largely unclear. Ig heavy chains are glycosilated mainly on the Fc portion and this is thought to be important in receptor binding and possibly control of clonal expansion. In MM tumor cells produce large amounts of a single Ig molecule. We compared glycosilation patterns in 18 IgG MMs and 19 matched controls by measuring levels of galactose and sialic acid moieties attached to heavy chains. IgG was purified using ammonium-sulfate precipitation and anion exchange chromatography, separated by denaturing electrophoresis and transferred onto PVDF membrane. Galactose and sialic acid moieties attached to heavy chains were detected using biotin-labeled RCA I and lectin, respectively. Galactosilation of MM chains was significantly less than that of normal controls (mean 283 relative units (RU), std. deviation 80 RU, vs. mean 352 RU, std. dev. 4 RU, p = 0.002). Sialylation was not different (mean 193 RU, std. dev. 83 RU, vs. mean 183 RU, std. dev. 30 RU), however some cases of MM had very low or very high sialylation. Neither galactosilation, nor sialylation correlated with clinical and biochemical parameters: sex, age, light chain type, disease status, disease duration, type of treatment, IgG or $\beta$2-microglobulin concentration. In MM the production of monoclonal immunoglobulin is accompanied by reduced galactosilation and in some cases aberrant sialylation. The clinical significance of these findings is presently unclear.

1359 PUBLICATION

## Cyclophosphamide, liposomal doxorubicin and dexamethasone (CLAD) is safe and efficacious in multiple myeloma

H. Szelényi, J. Siehl, H.D. Menssen, E. Thiel, U. Keilholz. [1]*Freie Universität Berlin, Universitätsklinikum Benjamin Franklin, Berlin, Germany*

Previously we showed that the combination of Cyclophosphamid, bolus AdriamycinO (doxorubicin) and Dexamethasone (CAD) is an efficacious therapy with a 75% objective response rate in patients with multiple myeloma. Data in the literature suggest that prolonged infusion of doxorubicin is even more efficacious. Liposomal encapsulation of doxorubicin (Caelyx®) shows a half time of 39 hours. Furthermore, studies show that Caelyx is less cardiotoxic as the free drug which is important for patients with multiple myeloma with a mean age in the 6th live decade. Therefore we initiated a phase I/II, dose escalating trial in patients with multiple myeloma with a CAD regimen in which doxorubicin is substituted by Caelyx (CLAD).

Treatment regimen was: Cyclophosphamid 200 mg/m$^2$ day 1–4, Liposomal Doxorubicin (Caelyx) in two dose levels day 1 and Dexamethasone 40 mg day 1–4. Dose levels of calyx are 10 mg/m$^2$ and 20 mg/m$^2$. Treatment was repeated every three weeks.

So far, 6 patients (3 women, 3 men) were included in our study on dose level 1. Median age was 68 years (range 61–83). IgA- myeloma was seen in 1 patient, IgG in 14 patients and light chain disease in 1 patient. All patients