184

RESULTS OF DIFFERENT APROACH TO THERAPY IN ADULT ACUTE LYMPHOBLASTIC LEUKEMIA

G. I. Kaletin. Russia, Moscow, Oncological research center

47 previously untreated pts received three different treatment programs depending on prognostic signs, which were immynological subtype, WBC count, and t(9;22). Group I (low rick, 16 pts) received induction therapy with Vcr, Pred, and Lasp (Lop). Group II (intermediate rick, 22 pts) Lop+Dauno. Group III (high rick, 9 pts) received ROAP. Consolidation therapy was also different in the three groups. CR rate was 88% in group I, 73% in group II, and 33% in group III. Median remission duration was 13,22, and 6 months, resp. 5 years disease-free survival was 23%, 43%, and 0%, resp. The results of the treatment in group II are better than in group I. More intensive induction and consolidation therapy in group II in our opinion accounts for it, and we decided to intensify treatment in the group I.

185

TREATMENT OF HAIRY CELL LEUKEMIA (HCL) WITH RECOMBINANT INTERFERON (rIFN) AND 2-DEOXYCOFORMICIN (DCF)

S. Lepkov
Cancer Research Center, Moscow, Russia

40 pts are included in this study, 34 males and 6 females aged 30 to 70 years (mean 48). Spleen was enlarge 25 pts, liver - in 15 pts. 32 pts had leukopenia Hairy cell count in blood varied from 12% to 98%. All pts had thrombocytopenia. Bone marrow in all cases contained a high percentage of hairy cells. 90% of pts had B-HCL, 1 pts - T-HCL, 2 - mixed B-T-HCL. All pts received rIFN 3-6 MU daily. The first sign of the treatment effectiveness appeared after a full dose 40-60 MU. It was an increase of platelet count. After 2 months of the treatment 32 pts achieved PR. None of the pts achieved CR before 4 months of trearment and a full dose of rIFN 120-150 MU. 20 pts achieved CR, 13 pts -PR, 4 pts died of infections during the treatment , and 3 were irresponsible. 5 pts, one with resistant to rIFN HCL and 4 with relapses of HCL received DCF, 4 mg/m^2 every other week. All pts achieved CR after 4 injections. CR has been more then 1 year in 4 cases. 1 pts had a relapse HCL and achieved tha 2-d CR after the treatment with DCF.

186

ACUTE LEUKEMIA IN ELDERLY.TREATMENT WITH ORAL IDARUBICIN.

M.Musso,E.Iannitto,G.Quintini,F.Porretto,R.Perricone,V. Abbadessa,A.Cajozzo.Chair of Hematology Palermo Italy.

We used oral Idarubicin(IDA,Pharmacia)to treat 13 elderly patients with AML(age range 67-81,M/F:6/7)nobody of whom could be treated with intensive therapy,11 patients were valuable. IDA was given orally at a dose of 20mg/m^2 for 3 days(q21-28) untill achieving a possible CR.Blood cells counts and renal-hepatic function tests were performed at least 3 times a week. ECG and echocardiography were done before each IDA take.Four patients achieved CR(1 after one single course)in 3 patients we noted failure of tratment,4 achieved PR.In all but one patient(non responder)the WBC count fell under 1000/mmc.The median duration of neutropenia was 8dd,While PLT count under 50 x10^3/mmc were registred for median 14dd.Nausea and vomiting were frequent but easily controlled with antimetics.No alteration of renal,hepatic function were registred,we noted low grade of cardiac toxicity(WHO1)in only 2 patients.It was noted 2 patients fever >38°C successful treat with antibiotics. We conclude that oral IDA induce responce rate like low dose of ARA-C with less toxicity,no cardiac toxicity and a better patients compliance.

187

ETHER PHOSPHOLIPIDS AND AZA-DERIVATIVES AS NEW ANTI-NEOPLASTIC DRUGS

Principe P., Coulomb H., Huchet M., Diomede [1]L., Suberville [2]AM., Broquet C., Mencia-Huerta J.M. and Braquet P. Institut Henri Beaufour, 91952 LES ULIS (France) ; [1]Istituto Ricerche Farmacologiche "M. Negri", 20100 MILANO (Italy) ; [2]Laboratoire de Cinétique et de Cultures Cellulaires, Hôtel Dieu, 75004 PARIS (France).

Ether phospholipids are new anti-neoplastic drugs that have been found to possess a direct cytotoxic and cytostatic effect against a variety of *in vitro/in vivo* tumor systems. These drugs are anti-invasive, can induce cell differentiation and are able to modulate the complex system of host defenses. The originality of their cytostatic action lies on the fact that, contrary to the majority of anti-cancer drugs, they do not interfere with the S- and the M-phase of the tumor cell cycle. The stathmokinetic analysis has pointed out a significant accumulation of tumor cells in the G_1 phase and a slow-down of the progression from late-S to G_2, resulting in a block in this latter phase of the cell cycle. The interaction between different ether phospholipids with eight chemotherapeutic agents on two human carcinoma cell lines has been evaluated using the isobologram analysis and a synergistic cytotoxic effect has been found between ether phospholipids', spindle-poisons and DNA-interactive drugs. The molecular mechanisms at the base of the tumoricidal activity of these new drugs are under active investigation. Experimental evidence has been cumulated on the fact that their tumoricidal activity is mediated by the cell membrane. The ability to induce apoptosis has been certified in different leukemia cell lines. A positive correlation has been found between the membrane cholesterol content and the sensitivity of leukemic and carcinoma cells to ether phospholipids cytotoxicity. Flow cytometric analyses have shown increased cellular accumulation of the anthracycline daunorubicin in both sensitive and resistant cell lines after ether phospholipid treatment. In resistant cells, this effect has been found independent of the presence of the P-glycoprotein in the membrane. These results indicate that the ether phospholipid tumoricidal action is closely linked with the membrane biochemical composition and that these new anti-neoplastic drugs are able to change the dynamic structural organization of the tumor cell membrane.

188

RB and P53 GENE PRODUCT EXPRESSION in LEUKEMIA

Sahin B. Seyrek E. Paydas S.
Cukurova Uni.Faculty of Med.Dept.of Oncology Turkey

In this study we looked at the expression of the P105-RB and mutant P53 gene product in peripheral blood cells of 51 acute and 16 chronic leukemia by immunocytochemistry using the anti-P105 MoAb and anti-P53 MoAb.

We found absence of or barely detectable levels of P105 in 8 of 35 AML,3 of 13 ALL, 5 of 8 CLL,and 4 of 5 CML.Mutant P53 presence was observed in 13 of 33 AML, 3 of 10 ALL,1 of 5 CLL,and none of 3 CML.Both P105-RB loss and mutant P53 presence were detected in 4 of 43 acute leukemia.Clinical parameters of RB(-) and/or P53 (+) leukemias were also correlated.

We conclude that cumulative role of these 2 tumor suppressor genes in leukemogenesis should be studied in larger groups with more advanced methods.

189

P53 and pGp EXPRESSIONS in ACUTE LEUKEMIA

Seyrek E. Sahin B. Paydas S. Ersoz C.
Cukurova Uni.Faculty of Med.Dept.of Oncology Turkey

The aim of this study was to correlate P53 gene mutations and pGp incidence with clinical parameters in acute leukemias.Blastic cells were seperated from blood samples by Ficall Hypoque and kept at -20 c.MoAbs(Novocastra) were used for P53 and pGp detection.Positivity rates were calculated by counting 100 cells on semears.16 cases were positive for P53 out of 37 acute leukemias(11 ALL,26 AML).Positivity was between 5-100% The pGp incidence was 16%(6 cases) for the same 37 cases.Positivty was between 30-100%.Cases(+) for pGp were all relapsed cases.Among the 9 relapsed cases (+)pGp incidence was 66%.Both P53 and pGp were positive only in 3 cases.We concluded that P53 mutations may play in leukemegenesis and pGp positivity in previously negative cases may indicate drug resistance and/or transformation to a more malignant clone.