841

FLUDARABINE IN THE TREATMENT OF REFRACTORY LYMPHOCYTIC LEUKEMIA (CLL) AND LOW GRADE LYMPHOMA (LGL).

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Twenty four patients with refractory CLL and advanced LGL were treated with Fludarabine. 10 of the LGL were in terminal leukemic phase. Fludarabine was given at a dose of 25-30 mg/m^2, I.V. daily for 5 days, q 28 days. All patients had received previous chemotherapy with multiple regimens. Patients received a mean of 4 cycles (1-9 range). 4 patients - one with CLL and 3 with NHL achieved CR, while 7 LGL patients and 3 with CLL had PR. 3 of the responders remain in CR, 16 - 30 months after completion of therapy. One patient underwent successful autologous BMT while another with CLL had marrow cryopreserved during CR. The drug was well tolerated and toxicity was mild. In 9 of the 122 cycles patients required hospitalization. In conclusion, Fludarabine is active in refractory patients with CLL and LGL and induces CR and PR in some. Fludarabine could be used as primary therapy in these disorders in the future.

842

SUCCESSFUL THERAPY IN HAIRY CELL LEUKEMIA PATIENTS TREATED WITH 2-CHLORODEOXYADENOSINE (2CdA) - SINGLE INSTITUTE EXPERIENCE.

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In recent years, 2 CdA has been used successfully to treat and cure hairy cell leukemia (HCL). This new agent, synthetized in 1980 is an adenosine analogue resistant to adenosine deaminase. The drug is given as a continuous I.V. infusion at 0.1 mg/kg/day for 7 days and has achieved excellent results in HCL. Since January 1991 we have treated 13 patients with HCL. Eight failed previous therapy with Interferon, 4 were splenectomized and 2 of these had received prior therapy with Interferon. Complete remission was achieved in 10 patients and PR in 2. Mean Hb levels increased from 10.8 g to 14.5 g/dl, ($p = 0.003$), mean platelet levels increased from 102 x 10^9/l to 210 x 10^9/l while the percentage of lymphocytes decreased from 56% to 27% because of recovery of granulocytes and monocytes. Side effects were minimal with transient leukopenia in 7, fever in 6 and 3 patients had documented infections which were easily controlled. Our results are similar to those reported in larger series from the USA and support the fact that 2-CdA therapy is probably the current treatment of choice for HCL.

843

TRANSFORMED CML: PATTERNS AND THERAPY.

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CML transforms into an acute leukemia 2-4 years after diagnosis.We report 50 patents who underwent blastic change after a median of 78 weeks. There were 4 unclassified,8 B-lymphoblastic and 38 acute myelogenous leukemias, including 31 myeloblastic, 3 promyelocytic, 1 myelomonoblastic, 1 erythroblastic and 2 megakaryoblastic leukemias. 22 patients developed new cytogenetic abnormalities in addition to being Ph$^+$.These included trisomy 8 (12), double Ph$^+$ (8), trisomy 19 (4), trisomy 21 (4) and triple Ph$^+$ (4). The overall median survival was 61 days. The 8 B-ALLs, treated as de novo ALL, survived a median of 75 days. Of the rest, 22 died untreated, 6 received combination daunorubicin, araC and thioguanine, 2 single agent mitoxantrone and 11 combination thioguanine, daunorubicin, araC, methotrexate, prednisolone, cyclophosphamide and vincristine. None of these combinations induced a remission with a median survival of 61 days.CML has a poor outlook terminating with an unresponsive acute leukemia

Lung Cancer

Lung Cancer – Small Cell

844

ETOPOSIDE/VINCRISTINE (EV) +/- CARBOPLATIN (C) IN EXTENSIVE STAGE SMALL CELL LUNG CANCER - A PHASE III-TRIAL

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Platin-derivates are some of the most active drugs in SCLC. To evaluate the role of Carboplatin in the treatment of extensive stage SCLC a prospective randomized trial comparing CEV vs. EV was performed.
Dosage and schedule: Treatment A: Carboplatin 300mg/m^2 iv. day 1, Etoposide 140 mg/m^2 iv. day day 1-3, and VCR 1,4 mg/m^2 day 1,8,15. Treatment B: Etoposide 200 mg/m^2 iv. day 1-3, VCR 1,4 mg/m^2 day 1,8 each every 4 weecks.
Results: Between 10/88 and 2/92 344 pts. were entered to the protocol. 317 pts. are evaluable for response and toxicity. Both groups are well balanced for prognostic factors. (A: 156 pts., B: 161 pts.)
Patient characteristics:
CEV/EV: Median age 58/62; Performance-status 80/80;
Mean cycles: 3,8/3,2.

Response: CR+PR: CEV 26,4% + 53,4%, total 79,8%
p= .001
EV 14,6% + 45,2%, total 59,8%
MST: CEV 10,0 mo. **1-year-survival:** CEV 41%
p= 0,19 p= 0,19
EV 9,0 mo. EV 34%
Toxicity: Hematological and non-hematological side effects are more pronounced in the CEV-arm
Conclusion: Response-rates are significantly better in the CEV arm. Median remission-duration and MST can be prolonged 1-2 months by CEV in comparision to EV, but without a statistically significant differance. According to 1- and 3-qear survival rates, there is a statistically significant advantage for CEV, esp. for patients with good PS, age < 60 yr, without distant metastases and with CR due to first-line therapy.

845

TWO DOSE LEVELS OF EPIRUBICIN IN COMBINATION WITH CIS PLATINUM AND VINCRISTINE /PEV/ IN THE TREATMENT OF SMALL CELL LUNG CANCER /SCLC/ - RESULTS OF A CONTROLLED STUDY.

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The aim of the trial was to study dose response relationship of 4-Epidoxorubicin (4-Epi) in combination with Cis platinum (DDP) and Vincristin (VCR).In a phase III randomized study 156 patients with untreated SCLC entered the study.Evaluable for toxicity and response were 138 pts.In arm A 4-Epi was given in the dose of 60 mg/m^2,DDP 60 mg/m^2 and VCR 1.4 mg/m^2 all day 1 (PEV 60).Arm B consisted the same dose of DDP and VCR but 4-Epi was given in high dose of 120 mg/m^2 iv.(PEV 120).Overall response (limited+extensive disease) was 49.3% in PEV 60 and 68.7% in PEV 120 arm ($P < 0.05$).In limited disease the overall response was 46% with PEV 60 and 66.7% with PEV 120 arm. The same difference was also observed in extensive disease ($P < 0.03$).However, in spite of more CRs in PEV 120 arm, there was no difference in recurrence free period and overall survival.Toxic side effects were moderate in both groups with slightly increased myelosuppression in PEV 120 arm. The results also showed that 4-Epi in the dose of 120 mg/m^2 could be safely used in combination chemotherapy of SCLC.