

correct management of this neoplasia with the help of two clinical cases observed in the last four years.

**Methods:** 2 young females of 32 and 39 years old were admitted to our Dept. in 1994 and 1997 respectively. The patients (pts) complained diffuse abdominal pain, nausea, anorexia and weight loss. The clinical examination underlined the absence of palpable masses and presence of hepatomegaly. Laboratory findings emphasized the following results: increased LDH > 700 U/L,  $\gamma$ -GT > 50 U/L, alkaline phosphatase > 250 U/L, VES > 50, HCV-RNA+ with normal values of CEA and  $\alpha$ FP. The thoracic and abdominal CT scan showed hypodense and diffuse masses of the liver in both pts. Finally, by means of an hepatic FNAB, the exact diagnosis was carried out. So, 8 cycles of CHOP chemotherapy were administered. Then, at the end of the scheduled cycles, pts received  $\alpha$ -2b Interferon (3 m.i.u.) 3 times at week for 6 consecutive months.

**Results:** An intensive follow-up consisted of clinical and laboratory exams every 3 months, hepatic US and/or CT abdominal scan every 6 months was established. After a follow-up of 36 months and 12 months respectively, pts are alive with no evidence of disease (100% CR).

**Conclusion:** this short report confirmed the importance of hepatic FNAB to achieve the correct diagnosis and showed that the adopted CHOP plus  $\alpha$ -2b Interferon chemotherapy was effective and well tolerated.

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PUBLICATION

### Retrospective evaluation of the risk profile in chronic myelogenous leukemia (CML) according to a new prognostic scoring system

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Several prognostic scoring systems have attempted to identify the risk factors for the predictions of overall survival at diagnosis of CML. Until recently, the most widely accepted was Socal's risk index, however, a new scoring system has been proposed in 1998 for patients treated with interferon alpha (IFN- $\alpha$ ) (Hasford et al, J Natl Cancer Inst, 90: 850). This system takes into account age, spleen size, percentage of peripheral blasts, eosinophils, basophils and platelet number. We undertook a retrospective analysis of a series of 71 Ph positive CML patients according to the new risk scoring system. Patients were stratified in low, intermediate and high risk group (n = 19, 16 and 36, respectively) with median overall survival of 92, 52 and 46.5 months respectively. In order to evaluate the predictive value of the new risk scoring system, we performed a univariate analysis so as to identify statistically significant associations between risk score and survival. Although the number of patients included in this analysis is not very large, a statistically significant association was found between low risk score and longer overall survival (p < 0.02). Furthermore, in the low- and high-risk groups, treatment with IFN- $\alpha$  was significantly associated with better outcome (p < 0.04 and <0.006, respectively) compared to other forms of treatment (hydroxyurea, alkylating agents). In all three risk groups, the type of bcr-abl chimeric transcript (b3a2 v b2a2) did not seem to affect prognosis. In conclusion, our analysis generally confirms that the new scoring system offers a reliable means for the estimation of overall survival in CML; however, it should be noted that its predictive value was more limited in the intermediate risk group. If the same results are repeated in further studies with larger number of patients, the new scoring system could be of special help for the application of risk-adjusted therapies and the identification of patients most likely to benefit from bone marrow transplantation.

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PUBLICATION

### Therapy of Morbus Hodgkin in one Pediatric Oncohaematologic Center in Ukraine

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**Purpose:** Modern Chemotherapy-Radiotherapy Strategy for treatment children and adolescents with Morbus Hodgkin was introduced to improve outcome for these patients.

**Methods:** Therapeutical Germ Protocol DAL-HD-90 was used in Pediatric Oncohaematologic Department in Kiev Regional Oncologic Dispensary for treatment of 34 patients (23 boys and 11 girls, median age 10 y 5 m with range 4 y-18 y 4 m) with initially diagnosed Morbus Hodgkin: Stage IIA was in 11, IIB-4, IIIA-8, IIIB-3, IVA-2, IVB-in 6 pts.

**Results:** 5-years pEFS for total group was 0.80 (SD = 0.1); 1 pt was NR, 4 pts relapsed, nobody died because of therapy complications.

**Conclusions:** Therapy results became dramatically better after introducing of modern principles in diagnosis and therapy. For further improvement of patients, outcome more accurate stratification and more detailed investigations are needed.

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PUBLICATION

### Induction of apoptosis by new alkylphosphocholines

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The aim of the study was to investigate the cytotoxic effects of erucylphosphocholine (EPC), erucylphospho-N,N,N-trimethylpropanolamine (EPC3) and octadecyl-(1,1-dimethylpiperidino-4-yl)-phosphate (ODPP) on human leukemic cell lines with (K-562, LAMA-84, BV-173 and CML-T1) or without (HL-60, THP-1, TMM, SKW-3 and EB-1) expression of BCR-ABL. EPC, EPC3 and ODPP showed relatively low IC50 values in BCR-ABL negative cells (about 5  $\mu$ M). However, all BCR-ABL positive cell lines were resistant (IC50 > 20  $\mu$ M). Following an incubation of 24 h, the APC caused oligonucleosomal DNA fragmentation typical for programmed cell death in HL60, SKW-3 and THP-1 cells. BCR-ABL positive cells, however, showed an apoptotic DNA ladder only after prolonged incubation (48 h) and following higher concentrations of the test compounds. Induction of apoptosis was confirmed by ELISA. Experiments with a cell-free system consisting of cytosolic fraction from treated and nuclei from untreated cells showed that DNA fragmentation was caused by cytosolic extracts from HL-60 and SKW-3 cells exposed to EPC in nuclei from K-562, LAMA-84 and SKW-3 cells. Thus, the induction of apoptosis is a common mechanism of the anti-leukemic activity of alkylphosphocholines. We suppose that expression of BCR-ABL is the main cause for the retarded apoptosis and resistance observed.

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PUBLICATION

### Beta-2-microglobulin elevated serum levels highly correlate with tumor burden and clinical response in newly diagnosed and relapsed Non-Hodgkin's Lymphomas treated with standard doses chemotherapy

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The role of beta-2-microglobulin as a prognostic factor in Non-Hodgkin's Lymphomas (NHLs) has been emphasized by many authors. We analyzed beta-2-microglobulin (beta-2-m) serum levels of 74 consecutive patients (PTS) affected by newly-diagnosed or relapsed low-grade (31) or intermediate-high grade (43) NHLs. All the patients have been treated with standard doses chemotherapy. Thirty PTS (40.5%) showed beta-2-m serum levels higher than 3 mg/L that we considered as the cut-off value. We analyzed the main prognostic factors of beta-2-m-positive (beta-2-m+) PTS according to the International Prognostic Index (I.P.I.) and compared them with those expressed by beta-2-m-negative (beta-2-m-) ones. Beta-2-m serum levels showed a high correlation with elevated LDH serum levels (p = 0.03) and stage according to Ann Arbor Classification (p = 0.0001), two clinical features currently used as markers of the tumor burden. The complete clinical remission (CCR) reached with standard front-line chemotherapy also correlates with the presence of normal serum levels of beta-2-m.

No correlation was found between beta-2-m serum levels and the others prognostic factors: age (p = 0.54), Performance Status (p = 0.078), extra-nodal sites of disease (p = 0.1), I.P.I. subgroups (p = 0.45). In conclusion, our data confirm that beta-2-m serum levels may play a role as a measurable marker of tumor burden and as a prognostic factor in NHLs.

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PUBLICATION

### Low dose Idarubicine, Vincristin, Prednisone, and G-CSF plus ATRA for the treatment of poor risk myelodysplastic syndrome (MDS)

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**Purpose:** The myelodysplastic syndromes (MDS) are heterogenous group of disorders with an invariably fatal outcome. Other than bone marrow transplantation, no treatment has been able to alter the natural history of MDS. Many of the drugs that have been evaluated in attempt to increase