t(13;14) in all 35 metaphases examined while the complex chromosome abnormalities often associated with MM were found in a part of these metaphases suggest that the two diseases were arising from the same neoplastic cell MM being a clonal evolution, probably related to the therapies that the patient had received for the CLL.

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IMMUNE THERAPY IN CHRONIC LYMPHOCYTIC LEUKEMIA: ALEMTUZUMAB (MABCAMPATH) (ANTI-CD52)

B.A.P. Laros-van Gorkom, P.W. Wijermans, P.F. Ypma, M.R. Schipperus

Hagahospital, Location Leyenburg, THE HAGUE, Netherlands

Backgrounds. Chronic lymphocytic leukemia (CLL) is the most prevalent leukemia in adults in The Netherlands. Recent developments with monoclonal antibodies offer new therapeutic options. Alemtuzumab (MabCampath™) is a monoclonal antibody aimed at CD52, which is present on both normal and abnormal B and T lymphocytes. It is indicated as third line therapy in the treatment of CLL, after failure of conventional therapy including fludarabine. The most important side effects of Alemtuzumab treatment are opportunistic infections (pneumocystes carinii pneumonia (PCP) and CMV pneumonitis). It is unclear whether these complications do indeed lead to problems in the treatment of CLL patients in the Netherlands. *Aims.* To gain insight in the use and complications of Alemtuzumab in the Netherlands. Methods. A questionnaire concerning the treatment of CLL patients with Alemtuzumab was made on the basis of the literature [1] and sent to 11 hospitals in The Netherlands Results. From 18-02-02 until 01-04-05 22 patients (mean age 64 years, 16 men, 6 women) with CLL RAI/BINET stadium IIA to IVC were treated with 26 treatments of Alemtuzumab according to schedule (starting dosages 3, 10, 30 mg, followed by 3 times per week 30 mg i.v./s.c. for 4-12 weeks). Patients had received a mean of 3 lines of previous therapy before starting on Alemtuzumab. The time from diagnosis until the start of Alemtuzumab treatment was 5.6 years (4.5) (mean, (SD)). The duration of treatment was 9 (3.4) weeks (mean, (SD)). Reason for early discontinuation of therapy was: fever and other side effects 20%, progressive disease (PD) 13%, complete response (CR) 13%, bone marrow toxicity 13%, other reasons 7%, unknown 33%. 27% of the treatments could be continued for the full 12 weeks. The most prevalent side effects were fever 73%, rigor 42%, dyspnea 19% and tiredness 15%. Infectious complications were pneumonia 26.9% (of which 1 PCP), sepsis 7.7%, herpes zoster 7.7%, sinusitis 7.7%, meningitis 3.8%, guillain barre 3.8%, others 15.3%. The response attained was CR 17%, partial response 35%, stable disease 30% and PD 17%. The duration of the response was 9.5 (7) months (mean (SD)). *Summary/Conclusions.* Treatment with Alemtuzumab is often discontinued prematurely. Therefore the maximal treatment effect cannot be reached. Fear of severe uncontrollable opportunistic infections seems unfounded.

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ANALYSIS OF RISK FACTORS OF 248 PATIENTS WITH B-CHRONIC LYMPHOCYTIC LEUKEMIA AT DIAGNOSIS

E.C. Cmunt,[1] M. Trneny,[1] J. Karban,[1] J. Salkova,[1] K. Michalova[1], Z. Zemanova,[1] L. Pavlistova,[1] J. Schwarz,[2] S. Pekova[2]

[1]*General University Hospital, PRAHA [2], Czech Republic;* [2]*Institute ofHaematology&Blood Transfusi, PRAHA, Czech Republic*

248 patients (139 men and 109 women) with B-cell chronic lymphocytic leukemia were evaluated at diagnosis with respect of clinical stage, CD38 and ZAP-70 expression, cytogenetic changes (by FISH method) and IgVH mutation status and impact of these for overall survival. In Rai 0 and I clinical stage were 203 patients (82,9%), in stage II were 25 patients (10,2%) and in stage III and IV were 17 patients (7,0%). CD38 expression was evaluated at 137 patients (55,2%), positive was at 49 patients (35,8%), negative was at 88 (64,2%) patients. ZAP-70 expression was evaluated at 109 patients (44% from the total number), positive was at 44 patients (40,4%), negative at 65 (59,6%) patients. From 160 evaluations of IgVH mutation status (64,5% of the total number of patients) 71 (44,4%) patients were non-mutated and 89 (55,6%) cases were mutated. From 192 evaluated patients (77,4% of the total number of patients) trisomy of 12 chromosome was present at 22 patients (11,5%), one case was borderline (0,5%), 13(q14) deletion was present at 107 cases (56,6%) out of 189 evaluated (76,2% of the total number of patients), 11(q23) deletion was found at 4 cases (12,9%) out of 31 evaluated (12,5% of the total number of patients), 11(q22.3) deletion was present at 13 cases (16,5%) out of 79 evaluated (31,9%) and 17(p13) deletion by 22 patients (11,4) out of 193 evaluated (77,8%). 48 patients died (19,4%), overall survival in 5 years was 83,5%, in 10 years 58,2%. According to our analysis sex (p=0,0002), Rai clinical stage (p=0,0002), IgVH mutation status (p=0,0001), 17(p13) deletion (p=0,09), CD38 (p=0,05) and ZAP-70 expression (p=0,02) revealed to be significant prognostic risk factors.

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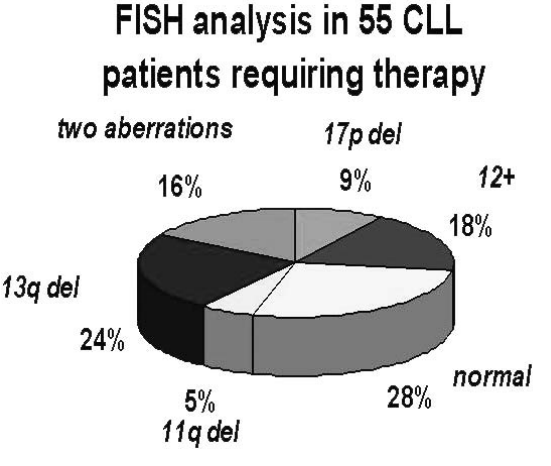
HALF OF CLL PATIENTS REQUIRING THERAPY DISCLOSE NORMAL FISH KARYOTYPE OR THE FAVORABLE 13Q DELETION

L. Shvidel, M. Shtalrid, J. Rosensaft, M. Rosless, M. Haran, A. Duek, E. Sigler, A. Klepfish, A. Berrebi

Kaplan Medical Center, REHOVOT, Israel

Chromosomal aberrations, detected by FISH, are considered as one of the most important prognostic factor in B CLL. Due to its expensive cost we chose to focus our analysis only on patients who required therapy. Fifty-five patients were studied, including 12 patients in stage Binet A and showing progressive disease. The lymphocytes were fixated for analysis before starting cytoreductive therapy. Examination included: 13q, 17p and 11q deletions and chromosome 12 trisomy. The results are presented in figure. The 17p deletions were found in 5 cases, including 2 active PLL patients and 3 CLL patients in stage Binet C. Trisomy 12 was found in 9 patients, all except one exhibited CLL/PL or PLL morphology. The 11q deletions were found in 3 Binet C patients. The 13q deletion was found in 13 patients including 4 in stage Binet A, 5 in stage B, 3 in stage C and 1 with aggressive PLL.



In addition, 13q deletion was associated with 17p del (2 patients), 11q del (4 patients) and 12 trisomy (3 patients). Single case disclosed 12+;11q del. Overall, chromosomal aberrations other than 13 del, were found in 4 out of 12 patients diagnosed in stage Binet A. FISH didn't show any aberrations in 15 cases. Considering the high prognostic significance of FISH analysis in CLL requiring therapy, it would be expected that patients in advanced stages and with progressive disease have unfavorable results. Nevertheless, our analysis in CLL patients requiring therapy showed that FISH results do not always correlate with the clinical stage of the disease. Part of the patients in stage Binet A had chromosomal aberrations supporting the need for therapy, but in other cases FISH revealed a favorable profile. Altogether, half of our patients disclosed either normal FISH results or the favorable 13q del. In conclusion, decision for treatment in patients with CLL cannot rely on FISH analysis alone and should be accompanied by additional prognostic factors.