

defined by  $A_{cy}/A_{sp} < 0.9$ ) in five of seven patients (eight of ten samples; mean  $A_{cy}/A_{sp}$  0.43 versus 0.95). Inhibitory effects of IL-12 on spontaneous in vitro apoptosis ( $A_{cy}/A_{sp} < 0.9$ ) were observed in three of seven patients (five of ten samples; mean  $A_{cy}/A_{sp}$  0.57 versus 1.2). IL-12 mediated inhibition of spontaneous cell death occurred only in patients showing a simultaneous IL-4 induced protection from in vitro apoptosis ( $p \leq 0.0385$ ). Three of four patients who developed progressive disease according to NCI criteria within twelve months after sample collection presented with both IL-4 and IL-12 mediated inhibition of in vitro apoptosis. In contrast, no significant inhibition of apoptosis by IL-12 alone, or both IL-12 and IL-4 was observed in patients with prolonged stable disease. The significance of our observation for the accumulation of malignant B lymphocytes in vivo is unclear. An increased susceptibility against IL-12 mediated inhibitory effects may be postulated for those B-CLL cells responding to IL-4. Whether the clinical outcome of patients with maintained versus lost in vitro responsiveness to inhibitory cytokine effects can help to define biological subgroups of B-CLL will be the subject of further studies.

1201

POSTER

### The vedex regimen: An effective and well tolerated palliative treatment for non-Hodgkin's lymphoma (NHL)

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**Objectives:** To evaluate the efficacy and toxicity of a novel weekly palliative chemotherapy regimen with vincristine 1 mg, epirubicin 30 mg/m<sup>2</sup> and dexamethasone 20 mg (VEDex) in relapsed NHL.

**Patients and Methods:** This was a retrospective study of 49 patients with NHL. The median age was 68 years (range of 34 to 88 years). 17 patients (34.7%) had low grade disease resistant to conventional alkylating therapy and 3 patients (6.1%) had transformed NHL. 29 (59.2%) had relapsed high grade NHL; of these 22 had poor performance status which precluded high dose chemotherapy and 7 were heavily pre treated. Responding patients received a total of 8 cycles of treatment but treatment could be repeated at a later stage if required.

**Results:** The overall response rate was 67.3%, 10 patients (20.4%) achieved a complete response and 23 (46.9%) a partial response. A further 16 patients (32.7%) had stable disease. 23 patients (46.9%) reported complete resolution of symptoms and 15 (30.6%) had partial resolution of symptoms. Grade III neutropenia was seen in 7 patients (14.3%) and grade IV in 1 (2%). Other significant toxicity's included nausea and vomiting grade II (4.1%), grade III (4.1%) and alopecia grade III (2%). Peripheral neuropathy of greater than grade I was not reported. The median survival from onset of treatment was 6 months. No patients died of treatment related toxicity.

**Conclusion:** VEDex is an effective and well tolerated palliative treatment for patients with relapsed NHL who have a poor performance status or who are heavily pre treated.

1202

POSTER

### The comparison of somatostatin receptor and 67-gallium scintigraphy in the staging of malignant lymphomas

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**Purpose:** We conducted a prospective blinded study comparing somatostatin receptor (SS-R) scintigraphy with gallium (GA) scintigraphy for staging of patients with malignant lymphomas.

**Methods:** SE-R scintigraphy was performed in 7 Hodgkin and 13 non-Hodgkin's lymphoma patients after i.v. injection of [111-In-DTPA-D-Phe-1]-octreotide (220 MBq). One week later high dose GA scintigraphy (296 MBq) was performed. The blindly read scans were compared with standard staging procedures.

**Results:** 16/20 patients were true positive and four were false negative on SS-R scintigraphy. On GA scintigraphy 9/20 patients were true positive and 11 false negative. With standard staging procedures 58 lesions could be identified. The sensitivity for SS-R scintigraphy was 40/58 (69%); 28/35 (80%) in the supra-diaphragmatic region and 9/18 (50%) in the infra-diaphragmatic region. The sensitivity for GA scintigraphy was 28/58 (48%); 19/35 (54%) in the supra-diaphragmatic region and 9/18 (50%) in the infra-diaphragmatic region. SS-R scintigraphy visualized 13 previously unknown lesions, four of these lesions were also visualized by GA scintigraphy.

**Conclusion:** The interpretation of the SS-R scan was easier because of its lower background radioactivity. The results of SS-R scintigraphy are at least comparable to GA scintigraphy.

1203

POSTER

### IDEC-C2B8-induced B cell depletion is not associated with significant immune suppression or infection

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**Purpose:** Short course (22 day) therapy with the chimeric monoclonal anti-CD20 antibody IDEC-C2B8 (rituximab) has resulted in a 50% ORR in evaluable patients with relapsed low-grade or follicular non-Hodgkin's lymphoma. Analysis of integrated safety data was performed to evaluate risk related to B cell depletion.

**Methods:** Of 282 pts from 5 single agent trials, 217 received 375 mg/m<sup>2</sup> IV qwk x4.

**Results:** Median circulating B lymphocyte counts dropped to zero following the 1st dose of IDEC-C2B8. CD3, CD4, CD8, and NK cell counts remained unchanged. B cell recovery began at 6-9 months and was complete by 12 months. Mean IgG and IgA levels remained normal. Mean IgM dropped transiently. 12% of pts had >50% drop in either IgG, IgA or IgM. Patients with low immunoglobulins were no more likely to develop infection. Only 2% of pts required hospitalization for infections (<1% vital, no fungal or parasitic) during treatment and 2% during the one year follow up period.

**Conclusion:** IDEC-C2B8 has significant clinical activity and the associated B cell depletion does not appear to increase the risk of immunosuppression or infection.

1204

POSTER

### Rescue treatment with etoposide, platinum, ifosfamide and dexamethasone for non-Hodgkin's lymphoma

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Approximately 50% of the patients with non-Hodgkin lymphoma (NHL) will relapse after first line treatments. We describe the results of the EPID rescue combination.

**Methods:** 32 patients (pts) with refractory or relapsed NHL were treated with the regimen: Etoposide 100 mg/m<sup>2</sup> on days 1, 2, 3 + Platinum 100 mg/m<sup>2</sup> divided in 3 days + Ifosfamide 5 g/m<sup>2</sup> divided in 3 days + Mesna 60% of the daily ifosfamide dose and Dexamethasone 20 mg x 3 days. The pts median age was 51 years. All pts received previously 1-2 chemotherapy regimens, the most common were CHOP and VACOP-B. Histology characteristics: high lymphoma in 27 pts and low-grade with transformation in 5 pts., bulky tumors in 80%. **Results:** After 140 delivered cycles 31 pts were evaluable for response and 32 for toxicity. Response rate: complete in 38.7% (12 pts) and 41.9% (13 pts) for an overall response of 80.6%. The median DFS was 13 months (range 2-42 months) with a median overall survival of 20 months (range 2-48 months). Toxicity in 140 cycles was: Grade (G) 3 neutropenia 12.5%, G4 19%, thrombo cytopenia G3 3.2%, G4 7.5%. Two pts died after septicemia and thrombocytopenia. Dehydration and electrolyte imbalance G4 in two pts.

**Conclusion:** The EPID regimen was highly effective with a prolonged survival rate. The most important toxicity was treatable neutropenia. We suggest the use of EPID scheme with colony stimulating factors.

1205

POSTER

### A decade of clinical investigation in elderly patients with non-Hodgkin's lymphoma: Results as reported in the literature

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**Purpose:** To explore the trends in the treatment of elderly patients with non-Hodgkin's lymphoma reported in last 10 years.

**Methods:** All relevant publications in MEDLINE, and the proceedings of the ECCO, ESMO, ASH, and ASCO meetings from 1987 to 1996 were categorized in 24 items, including study design (retrospective, phase II or (III), treatment (conservative or aggressive), characteristics of patients and IPI prognostic factors, response, survival, and toxicity.

**Results:** In 64 reports, we found 43 chemotherapy regimens and 90 treatment arms. The reports were retrospective in 22% of the cases, phase II trials in 64%, and randomized clinical trials in 14%. Most of the randomized

trials have been reported after 1994. When we compared the periods 1987–1991 and 1992–1996, we have observed an increase in the number of reports (19 vs 45), a trend for more aggressive treatments (50% vs 85%), an increase in the number of chemotherapy regimens studied (16 vs 32), and an 1 increase in the number of patients enrolled in clinical trials (872 vs 4462), but the median number of patients per treatment arm has remained small (31 vs 39). The median age of patients (74 yrs) and other clinical characteristics have not changed. Prognostic factors, according to the IPI have been reported completely in only 25% of the reports, and only 5% give details of concomitant diseases. Response rate was reported in 92%, but survival in 40%. Dose-intensity or delivery of cycles are shown only in 30%. Toxicities have been reported insufficiently, especially cardiac toxicity (20%) and mucositis (25%). Ten studies have evaluated the prophylactic use of cytokines, but none of them was randomized.

**Conclusions:** Most reports concerning NHL in the elderly are non-randomized phase II studies that use very diverse chemotherapy regimens and evaluate a small number of cases. Most investigations show response rates, but only a few show overall survival. There is a very low incidence of complete reporting of prognostic factors, response rate, or treatment toxicity. There is a marked need to perform controlled randomized trials in elderly patients with NHL that evaluate an adequate number of patients, in order to determine 1) treatment selection by prognostic factors, 2) the optimal treatment regimen(s), and 3) the need for the use of cytokines.

1206

POSTER

### Epidemiology of non-Hodgkin's lymphoma in Occidental Canary Islands

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**Purpose:** The present study review the patients's characteristics with Non-Hodgkin's Lymphoma (NHL) in an specific geographic area, Occidental Canary Islands (Spain), along 15 years.

**Methods:** From 1980 to 1994 we reviewed the cases of NHL collected from the two reference hospitals of this area, formed by four islands.

**Results:** We analyzed 525 patients. Mean age was 59 years (range 15 to 88). 283 males (54%) and 242 females (46%). Stage I 110 p (21%), stage II 88 (17%), stage III 88 (17%) and stage IV 218 (42%). Histology according to Working Formulation (WF) was: low grade 154 p (29%), grade intermediate 200 (38%), high grade 120 (23%), and 56 (11%) could not be classified. Average annual incidence per 100.000 in sequential time periods by age and gender was:

		All	15–34	35–54	55–74	<74
1981–84	All	5.5	1.2	4.5	15.4	12.3
	Male	6.8	1.7	4.7	21.4	15.8
	Female	4.3	0.6	4.3	10.4	10.6
1985–89	All	7.3	1.1	4.8	23.5	19.4
	Male	8.4	1.0	5.5	26.9	34.8
	Female	6.3	1.2	4.1	19.4	9.7
1990–94	All	8.0	1.6	6.1	20.2	24.4
	Male	8.0	1.4	6.3	22.2	28.3
	Female	8.0	1.8	5.9	18.4	21.9

17 years overall survival was 30%, median 5 years. Median survival by low grade, grade intermediate and high grade was 8, 5 and 1.5 years. 14 years overall survival was 34%, 30% and 20% respectively.

**Conclusion:** The NHL incidence in this geographic area is increasing. The frequency is higher in male older than 54 years.

1207

POSTER

### Results of radiation therapy and combined radio-chemotherapy in the treatment of the CB-CC non-Hodgkin's lymphoma

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**Purpose:** To evaluate the results of treatment of centrocytic-centroblastic Non-Hodgkin's lymphomas with special respect to recurrent disease and site of recurrence.

**Methods:** From 1978 to 1993 83 patients were treated with radiotherapy. 37 patients with localized disease were only irradiated, 46 patients with progressive disease underwent combined radio-chemotherapy. Standard dose applied was 26 Gy. In 27 cases an involved-field technique, in 56 cases an extended-field technique was used.

**Results:** After treatment 53 of 83 patients were in complete remission. 44 patients (53%) developed recurrent or progressive disease seven to 95 months after radiotherapy. 16 recurrences (36%) occurred within the primary target volume, 28 (64%) outside. The rate of recurrence was lower and the latency to recurrence prolonged after extended-field irradiation and chemotherapy. The overall five-year-survival rate was 66%, the tumor-free survival rate however only 25%.

**Conclusions:** The five-year-survival rate is increased after combined radio-chemotherapy and extended-field-irradiation. Extended-field-techniques are lowering the rate of local recurrences. According to the literature the dose has to be elevated to 36 Gy in order to achieve further improvements.

1208

POSTER

### Splenectomy in patients with non-Hodgkin's lymphoma

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**Purpose:** To evaluate the role of splenectomy in patients with non-Hodgkin's lymphoma (NHL) for diagnostic or therapeutic reasons.

**Methods:** Among 403 patients with NHL diagnosed and treated in our Unit during the last 17 years, splenectomy was performed in 24 (6%) patients. Group A: In 16 cases splenectomy was performed for diagnostic reasons. Group B: 3 patients were splenectomized for autoimmune hemolytic anemia (AIHA). Group C: 5 patients were splenectomized because of hypersplenism. There were 12 men and 12 women with a median age of 54 years (26 to 76 years). 17 patients were in advanced stages (III–IV). Histologically 14 patients had intermediate or high grade, while 10 had low grade NHL.

**Results:** In all patients of group A spleen was infiltrated by NHL, with a median weight of 1500 g, (range 700–2200 g). Liver and abdominal lymph nodes were infiltrated in 8/14 (57%) and 12/16 (70%) patients respectively. All patients of group B were classified in stage IV. In two of them the spleen was massively enlarged and infiltrated by NHL. In all patients of this group AIHA resolved after splenectomy. Hypersplenism was resolved in 4 patients after splenectomy, while the fifth patient died postoperatively. Surgical complications were observed in 5 (20%) patients, while 7 serious infections occurred in 6 patients, and one was lethal.

**Conclusions:** 1) Splenectomy is useful for diagnosis in some patients with NHL and splenomegaly. 2) In patients with NHL and AIHA unresponsive to other manipulations, splenectomy is very effective. 3) Splenectomy should be considered in all patients with NHL associated with hypersplenism. 4) Infections are common in splenectomized patients, and should be treated promptly and vigorously.

1209

POSTER

### Primary extranodal non Hodgkin's lymphoma of the head and neck (HN-NHL)

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**Purpose:** HN-NHL accounts 10–20% of all cases of NHL. Despite their frequency natural history and biological behaviour of these lymphomas is poorly understood. In this study we analysed our cases of HN-NHL diagnosed and treated in our Units during the last 17 years.

**Methods-Results:** Clinical and histological data from 114 patients with HN-NHL, were reviewed. There were 63 males and 51 females with a median age 56 years. The distribution among different anatomical sites was: tonsils 55 cases (48.2%), pharynx 18 (15.8%), mandible and gums 8 (7%), hard palate 7 (6.1%), nasal cavity 6 (5.3%), parotis 6 (5.3%), thyroid 5 (4.4%), larynx 2 (1.8%), miscellaneous 7 (6%). The patients were treated with radiotherapy alone (15 cases), combined chemotherapy (51) and combined modality (45). The disease was mainly localised (Stage I: 50.8%, Stage II: 34.4%). According to the WF histological classification 73 cases (64.1%) were intermediate, 28 (24.5%) high and 13 (11.4%) low grade. Complete remission was achieved in 97 (87.4%) patients. Patients were separated in two groups: Tonsillar NHL (55 cases) and NHL of all other sites of the HN (non-Tonsillar NHL, 59 cases). The patients with Tonsillar NHL did not differ significantly from the non-Tonsillar NHL in respect of the sex, age, stage, histological subtypes and treatment response. However the two groups differed in 3 respects: disease free period (DFP), overall