pts resistant to first, last, or all chemotherapy were 43%, 34%, and 32% respectively. In 23 pts relapsed after ABMT the ORR was 78%.

Conclusions: IDEC-C2B8 is well tolerated and does not impair marrow reserves. Thus, subsequent chemotherapy is not precluded. Outpatient therapy is feasible and is completed within 22 days (days 1, 8, 15, and 22). IDEC-C2B8 is safe and effective in the treatment of pts with R-LG/F NHL.

1180 ORAL

First demonstration of anti-lymphoma activity of BCL-2 antisense molecule-G3139; Results of phase I/IIA clinical trial

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Introduction: It has been well known that T14/18 translocation in follicular lymphoma up-regulates BCL-2, leading to continued expression of BCL-2 protein. Upregulation of BCL-2 leads to extended survival of the cells and increased chemoresistance. Clinical trials demonstrated correlation between BCL-2 expression and poor clinical prognosis in an intermediate and high grade lymphomas. G3139 is an all-phosphorothioate 18mer oligonucleotides targeted to the first six codons of the BCL-2 mRNA. It has been shown to specifically down regulate BCL-2 *in vitro* and to have dose dependent activity in mice models of human lymphoma as well as other xenograft models of solid tumours.

Methods: The Lymphoma Unit at the RMH performed the first Phase I trial in all grades NHL pts who relapsed following several previous conventional chemotherapy regimens and who expressed BCL-2. Replicating preclinical xenograft model, the patients received G3139 as a continuous, subcutaneous 14 day infusion. The doses were escalated according to EORTC scheme and safety as well as efficacy measured using standard evaluation criteria.

Results: Until early February 1997, 13 pts were entered in 6 dose escalation cohorts up to a dose of 147.2 mg/m^2/day. Based on excellent systemic tolerance the escalations were made in 100% increments. At the 6th dose level, reversible grade 3 thrombocytopenia was observed in 1 pt. Mild topical, infusion site irritation which was generally acceptable but two pts had more severe reversible reactions which were not dose dependent. Blood levels of two pts at 5th escalation level approximated concentration effective in *in vivo* models of lymphoma. In the first 9 pts, 4 pts demonstrated improvement in disease status as defined by clinical and.or laboratory parameters including decrease in BCL-2 protein. One of those 4 pts demonstrated minor tumour response. Another patient on the higher dose, who failed 4 prior therapies, with follicular grade II lymphoma, stage IVB, developed complete clinical and radiological response of 30+ week duration.

Conclusion: We conclude that antisense approach to BCL-2 constitutes a potentially important treatment modality in NHL, leading to responses in poor prognosis patients at doses causing low toxicity. The trial is continuing and the full update will be presented.

1181 ORAL

Management of stage I–II primary gastric non MALT-type lymphoma

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Purpose: Some therapeutic aspects of primary gastric non MALT-type lymphoma remain undefined. Impact on survival of gastrectomy as exclusive treatment, role of adjuvant chemotherapy (CHT) or radiotherapy (RT), use of RT in stage II and conservative treatment without gastrectomy were evaluated in a retrospective series

Patients and Methods: 136 pts with primary gastrointestinal NHL were reviewed. Pts with MALT lymphoma (n = 32), stage IV (n = 9) or extragastric sites (n = 9) were excluded. Study group consists of 86 pts: 43 with stage I, 23 with stage II_1 and 20 with stage II_2-disease. Median age was 62 ys (range 25–85). Seventy-three cases had intermediate- or high-grade lymphoma (IG-HG). Sixty-eight pts were submitted to surgical resection: as exclusive treatment (S) in 18 cases, followed by CHT (S-C) in 26, by RT (S-R) in 6 or by CHT and RT (S-C-R) in 18 cases. Eighteen pts did not undergo surgical resection, receiving only CHT followed or not by RT (conservative treatment).

Results: Sixty pts (70%) are alive (58 NED) at a median follow-up of 57 mo. Nineteen pts (22%) relapsed, 17 pts (20%) died of NHL and of 9 other causes (6 NED). There were no differences in relapse rate nor survival among pts with stage I treated with S alone, with S plus adjuvant CHT/RT or with conservative treatment. Partial or total gastrectomy showed similar relapse rate and survival among pts submitted either to S alone (p = 0.16) or to S followed by CHT and/or RT (p = 0.13). Addition of adjuvant CHT in pts with stage II and IG-HG significantly improved survival (56 mo, p = 0.01) in comparison to S alone (51 mo). Pts treated with S-C survived longer (62 mo) than pts submitted to S-R (9 mo, p = 0.009). Addition of RT to S did not improve local control nor survival (p = 0.16). S-C showed similar relapse rate and survival (62 mo) to S-C-R (73 mo, p = 0.24). Conservative treatment was associated to longer survival (67 mo) than S alone (51 mo) in pts with stage II-disease (p = 0.01). Conservative treatment showed a similar survival (66 mo) to S-C or S-C-R (57 mo, p = 0.23). Independent prognostic factors were age (p = 0.02), systemic symptoms (p = 0.009) and LDH level (p = 0.0006). Treatment modality showed prognostic value only among pts with stage II (p = 0.02).

Conclusions: Results with surgical or conservative treatments are excellent for pts with stage I. Extension of gastrectomy seems not to influence survival. CHT significantly improves survival in pts with stage II and IG-HG, and it should be preferred to RT as adjuvant therapy. Addition of RT to S or to S-C seems not to improved outcome. Since conservative treatment with CHT followed or not by RT obtains similar survival to S-C or S-C-R, surgical treatment should be indicated only for pts with high risk of bleeding or perforation with the aim to avoid the late-morbidity associated to gastrectomy.

1182 ORAL

Extended field (EF) and total central lymphatic (TCL) radiotherapy for early stages nodal centroblastic-centrocytic (CB-CC) lymphomas

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Purpose: A prospective multicenter trial was performed to evaluate survival and prognostic factors for patients with nodal cb-cc lymphoma in stages I–IIIA (≤5 involved regions) after EF and TCL radiotherapy.

Methods: 117 adults with clinical stage (CS) I–IIIA nodal cb-cc lymphoma were recruited. Patients with mediastinal or retroperitoneal stage I/II or stage IIIA lymphoma received TCL, the others EF radiotherapy. The whole abdomen was irradiated to 25.5 Gy (1.5 Gy/f), the mantel to 26 Gy (2 Gy/f); 5x2 Gy boost to macroscopic tumour. Age: 20–79 years; CS I/II/IIIA: 60/40/17; med. follow-up: 68 m.

Results: Overall survival at 8 years was 86%. The probabilities of nodal and disseminated extralymphatic relapses were 32% and 9% at 8 years. The dominant adverse prognostic factor for nodal in-field recurrences was a dose deviation below 80% of the prescribed dose (15 patients). After EF irradiation, patients in stage I had a significantly lower risk of nodal recurrences in adjuvant irradiated than in unirradiated lymph node regions. Acute toxicity was moderate.

Conclusion: This trial shows a steep dose-response relation between 26 and 36 Gy for cb/cc lymphoma. Adjuvant irradiation reduced the risk of nodal relapses per lymph node region. A randomised study of TCL vs. EF radiotherapy is in preparation by this group.

1183 ORAL

Quality control program of radiation therapy in EORTC H8 protocol: The French centers experience

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Rationale: The EORTC H8 protocol for early stage Hodgkin's disease include a precise definition of target volumes and dose. The aims of this study is to ensure that the radiation treatment effectively done is those required by the protocol.

Material and Methods: Each patient technical record was reviewed by all the radiation oncologists involved in the protocol of a given region (Paris, Lyon et Nancy), with a careful review of initial CT scans, simulation films, port films and radiation therapy data. For each target volumes, the quality of balistics (particularly the shape of the blocks) was judged adequate, doubtful or non adequate; and dose evaluated with DIF: DIF = (Dose received – dose provided by the protocol)/Dose received* 100.

Results: 161 patient records have been reviewed, 102 treated in involved fields (IF) and 59 with a subtotal nodal irradiation (STNI). We noticed

51 (31.6%) deviations in ballistics, with **22 (13.6%) major deviations.** Some of these major deviations were voluntary (block of the upper neck in case of no cervical involvement), most of the others were due to an incomplete coverage of the upper mediastinum and/or the hilar nodes areas. Considering the doses, **a major deviation (DIF ≥ 10%) was observed in 39.7% of the patients.** Targets inadequately exposed were cervical nodes (57%), upper mediastinum (13%) and lower mediastinum (30%). Type of irradiation (STNI or IF) did not influence the rate of protocol violations.

Conclusion: a quality control program seems mandatory in multicenter trials of Hodgkin's disease. This type of review is one of the best school for radiation oncologists.

1184 ORAL

Somatostatin receptor scintigraphy for the initial staging of Hodgkin's disease

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Purpose: Exact staging is important for the prognosis and treatment of patients with Hodgkin's disease (HD). In a prospective blinded study somatostatin receptor (SS-R) scintigraphy was compared with conventional staging methods for initial staging of patients with newly diagnosed HD.

Methods: 126 Consecutive patients underwent scintigraphy after i.v. injection of [111-In-DTPA-D-Phe-1]-octreotide, 220 MBq. SS-R scintigraphy and conventional diagnostic tests were interpreted independently and the results compared.

Results: The patient-based analysis yielded an overall sensitivity of 99% (125/126). In 28 patients (22%) the clinical stage was altered because of the result of SS-R scintigraphy. As a result the treatment plan was changed in 18 patients (14%). The lesion-based analysis showed an overall sensitivity of 94% (452/483). The sensitivity in the supra-diaphragmatic region was 98% (415/423) and 59% (32/54) in the infra-diaphragmatic region. In 4 lesions a false positive uptake of radioactivity was observed.

Conclusion: SS-R scintigraphy is positive in nearly all patients with newly diagnosed HD and appears to disclose sites of disease not revealed by conventional diagnostic tests. This new imaging modality provides a useful method of diagnostic evaluation in patients with HD.

1185 ORAL

Four cycles of ABVD followed by involved field irradiation (IF-RT) is the treatment of choice for early-stage Hodgkin's disease (HD): 5-year results of a randomized trial

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In February 1990 we started a prospective randomized trial with the aim to assess the relative role of subtotal nodal (STNI) vs IF-RT after 4 cycles of ABVD in early stage HD (I bulky and/or B; IIA, IIA bulky, IIEA). The doses of RT ranged from 30 to 36 Gy to uninvolved and involved sites, respectively. A total of 114 consecutive patients staged without laparotomy are presently evaluable after a median follow-up of 42 months. Patient characteristics were well balanced between the two groups. Overall, 20% of the patients presented with bulky HD and 77% with NS histology. The median age was 28 years (range 17–64).

The actuarial 5 years results were as follows:

(%)	ABVD→IF-RT	ABVD→STNI
Complete Response (CR)	98	100
Freedom from Progression	94	95
Overall Survival	96	100

The majority of patients were in CR after ABVD, while only 8% who were partial responders achieved CR at the end of the combined therapy.

Treatment was completed within a median of 6 and 7 mo (range 5–9) respectively for the IF-RT and STNI arm and ABVD dose-intensity was 0.84. Treatment was well tolerated. Two male patients developed acute myocardial infarction (AMI): one pt during the second ABVD course and died, the other pt 12 mos from the end of therapy and is still alive. No other severe sequelae have been so far documented. Only 14% of men resulted azoospermic and 3% of women became amenorrheic. Present results confirm our preliminary observation and indicate that short-term ABVD followed by IF-RT is the treatment of choice for clinically staged favorable or unfavorable early HD.

1186 ORAL

Alternating ChlVPP/PAB1OE is better than PAB1OE alone as initial chemotherapy for advanced Hodgkin's disease (HD): First results of a British National Lymphoma Investigation (BNLI)/Central Lymphoma Group (CLG) study

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This BNLI/CLG trial commenced in October 1992 and was prematurely concluded in April 1996 after the first interim analysis.

Objective: A randomised comparison of anthracycline-based chemotherapy PABlOE with alternating chemotherapy ChlVPP/PABlOE in advanced HD.

Patients and Methods: 682 patients (461 BNLI, 221 CLG) were randomised to either ChlVPP/PAB1OE (chlorambucil, Velbe, procarbazine, prednisolone alternating with prednisolone, Adriamycin, bleomycin, Oncovin and etoposide) or PABlOE alone.

Results: 604 patients are so far evaluable for response and survival analysis. The patient characteristics were balanced between the two treatment arms. In the ChlVPP/PABlOE arm the complete remission and freedom from progression rates are significantly higher (75% vs 60% and 72% vs 52% at 2 years, respectively). At present there is no significant difference in the overall survival between the two arms. There was significantly more grade III, IV toxicity for myelosuppression and infection in the ChlVPP/PABlOE arm.

Conclusion: Alternating ChlVPP/PABlOE is better than PABlOE alone as initial chemotherapy for advanced HD and will be a 'standard' therapy arm in the next United Kingdom Lymphoma Group randomised study.

1187 POSTER*

CD22 as target for radioimmunotherapy of hematological malignancies of B-cell origin (non-Hodgkin's lymphoma, acute lymphatic leukemia and macroglobulinemia)

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Purpose: The aim of this ongoing study is to evaluate the therapeutic potential of the ^{131}I-labeled anti-CD22 murine monoclonal antibody, LL2, as well as its humanized form (hLL2) in chemorefractory hematological malignancies of B-cell origin.

Methods: 21 patients with Non-Hodgkin's lymphoma (NHL) were treated with non-myeloablative, 3 with potentially myeloablative doses of ^{131}I-labeled LL2. A patient with acute lymphatic leukemia (c-ALL) who had failed 6 high-dose chemotherapies received a myeloablative dose of ^{131}I-labeled hLL2 IgG with allogenic stem cell transplantation. A targeting study was performed in a patient with macroglobulinemia.

Results: At mean tumor/whole -body radiation dose ratios of 9.6 ± 4.4, six of 17 assessable NHL patients experienced objective responses (complete and partial remissions). Although responses were seen at very low activities (complete remissions at ≤8 mCi), response rates increased with higher doses (66% CRs in the myeloablative trial). At a red marrow dose of 30 Gy (whole-body dose 3.5 Gy), the ALL patient went into complete remission. Excellent targeting was seen in macroglobulinemia. No second-organ toxicities were observed other than transient myelosuppression.

Conclusion: Radiolabeled LL2 is a promising agent for the treatment of NHL and leukemias of B-cell origin. Further clinical trials are ongoing. *(Supported in part by DFG Grant Be 1689/1-1/2 and USPHS Grant CA 39841 from the NIH.)*

*indicates Poster Discussion