the serum levels of lactate dehydrogenase (LDH) and 
$\beta_2$-microglobulin ($\beta_2$m), as shown in Table 2. Of all 
the serum factors studied, i.e. the sCD and the usual 
serum markers (LDH, $\beta_2$m, albumin, uric acid and C- 
reactive protein), sCD25 also showed the strongest 
correlation with tumor burden (data about albumin, 
uric acid and C-reactive protein are not shown in 
Table 2).

In conclusion, serum levels of sCD25, sCD8, 
sCD54 and sCD44 are roughly proportional to the 
burden of neoplasia, but sCD25 is clearly more sen-
sitive as a marker of tumor burden than others sCD. 
sCD25 is also clearly a more sensitive marker of 
tumor burden than usual serum factors. Measure-
ments of sCD25 can be indicated for stage assess-
ment in all patients with NHL.

Funding
This work was supported by grants XUGA90204A92 and 
XUGA90202A94 from the “Conselleria de Educación y 
Ordenación Universitaria de Galicia”.

Key words
Serum markers, tumor burden, sCD25, sCD8, sCD23, 
sCD54, sCD44, non-Hodgkin's lymphomas.

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Thyroid volume is progressively reduced as a 
sequela of neck irradiation for childhood 
Hodgkin’s disease

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Thyroid volume reduction was observed, among 25 sub-
jects off-therapy after Hodgkin’s disease. The volume 
reduction was related to dose (p=0.014) and time from 
radiotherapy (p=0.01). The correlation was very spe-
cific since all patients with reduced volume had 
hypothyroidism, but not very sensitive since 25% of sub-
jects with thyroid dysfunction had normal gland volume.

As the thyroid gland is frequently within the field of 

Figure 1. Regression line and 95% CI of the thyroid vol-
ume measured by us in patients evaluated at different 
times after completion of treatment for childhood Hodgk-
in’s disease.
None of the patients developed symptoms related to thyroid dysfunction or overt thyroid enlargement; one patient had a single thyroid nodule and regional lymph node enlargement. Thyroid function (FT4, T4, FT3, T3, basal and stimulated TSH) was normal in 9 of the 25 patients (36%), including 6 of the 22 (27%) who had received neck irradiation and 3/3 patients not irradiated (Table 1); 8 patients (32%) had low FT3 and FT4 levels, with increased basal TSH. Increased TSH response to TRH was present in 7/8 subjects. In 6 cases, thyroid replacement therapy was given, another became euthyroid and the other is still under evaluation. The remaining 8 patients (32%) had low FT3 and FT4 levels, with normal basal TSH. After TRH stimulation, TSH response was raised in only two of these eight.

Ultrasound study. Sixteen patients (64%) had a normal thyroid, 9 had parenchymal cysts (n=4) or inhomogeneity (n=5); none of the patients showed parenchymal nodules. Thyroid volume was inferior to age-standardized volumes in 9/25 patients (36%) (Table 1). Thyroid volume was similar in male and female patients, and in patients older or younger than 15 years at the time of assessment. Although patients with low FT4 and high TSH values tended to have a lower thyroid volume, the difference was not statistically significant. Conversely, thyroid volume was significantly lower in patients with a radiotherapy dose >20 Gy and in patients off-therapy for >5 years. In the regression analysis none of the following were significantly associated with a lower thyroid volume: sex, radiotherapy site, radiotherapy dose (as a continuous variable), age at completion of treatment and age at current evaluation, levels of free T4 or of TSH, while time off-therapy, radiotherapy dose (cut-off 20 Gy), and, marginally, chemotherapy were significant. In the multivariate analysis only time off-therapy remained significantly associated with thyroid volume (p=0.01). This model showed that thyroid volume tended to decrease the longer the time since completion of treatment (Figure 1) and the more aggressive the chemotherapy and radiotherapy used.

In conclusion, thyroid ultrasound follow-up study for screening of thyroid nodules may provide additional information on thyroid volume, and this may be related to thyroid function. The thyroid volume was significantly inferior to age-standardized in 36% of the patients. Time elapsed from treatment completion was the only independent risk factor for this event.

<table>
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<th>Pts.</th>
<th>Sex/age</th>
<th>Chemotherapy</th>
<th>RT dose on neck</th>
<th>Laryngeal protection</th>
<th>Age at evaluation</th>
<th>FT4 (nv 7-19 pg/mL)</th>
<th>FT3 (nv 2.3-4 pg/mL)</th>
<th>Basal TSH (nv 0.3-3.8)</th>
<th>Stim. TSH (peak)</th>
<th>Thyroid volume (mL)</th>
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ABVD = adriamycin + bleomycin + vinblastine + imidazole carboxamide; OPP = nitrogen mustard + vincristine + procarbazine + prednisone; OPPA = vincristine + procarbazine + prednisone + adriamycin; COPP = vincristine + procarbazine + prednisone + cyclophosphamide; CEP = CCNU + etoposide + prednisone; *on replacement therapy with thyroxine; ° neck was irradiated twice, once during front-line mantle irradiation, and again after disease relapse.
Chlorambucil synergizes with purine analogs in inducing in vitro cytotoxicity in B-cell chronic lymphocytic leukemia

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*Centro Trapianti di Midollo Osseo e Terapia Sovrammassimale Emato-Oncologica, Divisione di Ematologia; °Centro per le Microcitemie e Biologia Molecolare, Dipartimento di Emato-Oncologia, Azienda Ospedaliera Bianchi-Melacrin-Morelli, Reggio Calabria, Italy

Combinations of different drug concentrations of CLB+FAMP and CLB+2-CDA were synergistic in, respectively, 42.9% and 34.8%. At leukemic cell survival \( \leq 50\% \), 16.4% and 23.4% of all combinations were synergistic in the 2-CDA and FAMP groups, respectively. A significantly higher mean value of antagonistic interactions was observed in the 2-CDA group (p=0.037).

Fludarabine (FAMP), 2-chlorodeoxyadenosine (2-CDA) and chlorambucil (CLB) induce apoptosis in chronic lymphocytic leukemia (CLL) B-cells.1,2 In this study we examined whether CLB improved in vitro CLL cell chemo sensitivity to either FAMP or 2-CDA. The results indicate that CLB synergizes in vitro with both purine analogs.

Samples from 23 CLL patients were tested. Lymphocytes were separated as previously described.3-5 CLB (Sigma, St Louis, Mo, USA), FAMP (Fludara, Schering AR, Germany) and 2-CDA (Leustatin, Ortho Biotech, USA) were employed at described concentrations.3-5 MTT assay was performed as previously described.3-5 The lethal dose (LD)\(^{50}\) values, leukemic cell survival (LCS) and drug interactions were calculated by home made software.3-5 FAMP-LD\(^{50}\) values were significantly lower with 100 µg/mL concentrations of CLB; conversely higher 2-CDA-LD\(^{50}\) values were observed with 0.01 µg/mL of CLB (Figure 1). The interactions between CLB and either 2-CDA or FAMP, tested in respectively 420 and 525 combinations, were synergistic in 146 (34.8% of the total) and 225 (42.9% of the total) (Table 1). Similar percentages of additive interactions (15.7% and 18.8%) were detected with both purine analogs, while a higher percentage of antagonistic interactions was observed among the 2-CDA group. At LCS \( \leq 50\% \), 23%