

Background. Previous results have suggested that ex vivo drug sensitivity test results are independent prognostic or predictive factors for subsequent patient response in chronic lymphocytic leukaemia. **Aims.** In order to determine its accuracy at predicting response and survival, drug sensitivity is being tested both at initial entry (closed October 2004) and at second randomisation (still open) in the UK Leukaemia Research Fund (LRF) CLL4 trial. **Methods.** At first randomisation, blood specimens were sent to Bath for drug sensitivity testing: initially by DiSC (Differential Staining Cytotoxicity) assay; subsequently by its development, the TRAC (Tumour Response to Anti-neoplastic Compounds) assay. Ten drugs were tested including chlorambucil, fludarabine and mafosfamide (used in vitro in place of cyclophosphamide). LC90s were calculated. Patients were randomised into Trial arms to receive chlorambucil (Chl), fludarabine (Flu) or fludarabine+cyclophosphamide (FluCy) in the ratios 2:1:1. Numbers of patients with any versus no response were compared. 2P is by Fisher's exact test. **Results.** From 777 randomised, LC90 results from 442 patients could be compared with subsequent patient response. Definitions of test-sensitive were LC90s of ≤ 6.3 ug/ml for chlorambucil, and ≤ 10.0 ug/ml for both fludarabine and mafosfamide. No difference in average drug sensitivity was found between Trial arms. Results are presented in the Table. All differences between response rates in the test sensitive and resistant groups were highly statistically significant. For instance, for those treated with Flu or FluCy, 90.7% (95% confidence interval (CI) = 86.8-94.6) of test-sensitive patients responded compared with 22.2% (3.0-41.4) test-resistant patients. **Conclusions.** At diagnosis of CLL, even within a group of patients with a high clinical response rate, ex vivo drug sensitivity can be used to identify a proportion of patients with a significantly poorer probability of clinical response. TRAC results predict better for patient response to fludarabine (+/- cyclophosphamide) than for response to chlorambucil.

Table 1. Comparison of ex vivo drug sensitivity with subsequent patient response (numbers of patients)

Trial arm	No.	Test sensitive		Test resistant		Odds ratio (95% CI)	2P
		Response	No response	Response	No response		
Chl	210	141	45	9	15	5.2 (2.1-13)	0.0004
Flu+FluCy	232	194	20	4	14	34.0 (10-113)	<0.00001
Total	442	335	65	13	29	11.5 (5.7-23)	<0.00001

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COMPARISON OF EX VIVO DRUG SENSITIVITY BY TRAC ASSAY AND PATIENT RESPONSE IN THE UK LRF CLL4 TRIAL.

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