4. **FURTHER DATA SHOULD BE SUPPLIED TO ESTABLISH LONG-TERM EFFICACY**

Response

The original Product Licence application contained data from 124 patients treated with a single course of cladribine and evaluated up to 30th September 1991. The most recent efficacy and safety update, dated February 1994, includes data from 30th September 1991 until 30th June 1993 for the 124 patients initially evaluated (Appendix 7).

The updated information collected in 1993 extended the maximum duration of follow-up to 7.2 years; the median duration of follow-up was three years for responding patients and 2.4 years for non-responders. Previously the median duration of follow-up for responding patients valid for efficacy was 1.3 years and one year for non-responders. 77% (72/93) of patients valid for efficacy who were considered to have been responders as of 30th September 1991 still had a documented complete response, good partial response or partial response as of 30th June 1993. 90% of patients valid for efficacy (84/93) were still documented to have a clinical response. Of the 21 patients (of 93 original responders valid for efficacy) who had responded in September 1991, but in whom clinical and/or pathological response was not maintained in June 1993, 12 patients (13% of original responders) had only pathological evidence of relapse (all had normal complete blood counts), three had evidence of clinical relapse only (3% of original responders) and 6 had evidence of both pathological and clinical relapse (6.5% of the original responding population). A table showing duration of follow-up and response rates is presented overleaf (Table 8).

Seven of the patients who relapsed were re-treated with cladribine with some success. Complete clinical and pathological responses were achieved in three patients and clinical responses were attained in four patients. Thus, re-treated patients appeared to be capable of some response to second courses of cladribine.

Of the 14 patients who failed to respond to a single course of cladribine, eight patients received additional treatment and six received no further treatment. Of the eight that were treated, six received at least one additional course of cladribine but none of the six showed any response to that second course of therapy.

In summary, analysis of efficacy data available after a doubling of the median follow-up period for the 124 patients originally presented in report MR92049, reveals that a single course of therapy with cladribine is capable of producing continued complete, good partial and partial remissions that are long-lasting.

TABLE 8

Summary of Duration of Follow-up and Response Status as of 30th June 1993 in the 124 Patients in the Pivotal Studies

Response on or before 30th September 1991	N	Median duration of follow-up in months (min-max)	Status as of 30th June 1993			
			No change	Clinical relapse	Pathological relapse	Both clinical and pathological relapse
Complete response (CR)	70	36 (4-49)	60	1	7	2
Good partial response (GPR)	13	35 (8-60)	8	-	1	4
Partial response (PR)	10	48 (35-88)	4	2	4	-
CR/GPR/PR[a]	93	36 (4-88)	72	3	12	6
No response	13	29 (1-39)	13	-	-	-
Non-evaluable at 30th June 1993	18	-	-	-	-	-

[a] All patients with complete, good partial or partial response.