Utility Measurement Study for Patients with Chronic Lymphocytic Leukaemia: Interim Report

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Aims of the Study

The purpose of this study is to estimate the health related quality of life of patients with chronic lymphocytic leukaemia (CLL). These data are being specifically collected to support the development of an economic model designed to compare treatments for CLL. The economic model will be designed to meet the requirements of NICE and as such will estimate benefit for different treatments in terms of the cost per quality adjusted life year (QALY). This observational study is designed to capture health related quality of life and utility data regarding the impact of CLL.

Methods

Participants

To date, two clinical sites have recruited 11 patients who are currently receiving therapy or have finished therapy and who have undergone an assessment of treatment response. These patients were classified in 6 CLL response states (complete responder, partial responder, progressive disease, stable disease (neither response nor progression), treatment failure or currently on treatment). The patients

were then further classified into progression free survival (stable disease, complete and partial responder and on treatment) or disease progression. The participants' socio-demographic details can be found in Tables 1a & 1b.

Design and Apparatus

A cross-sectional, single administration, quantitative questionnaire based study was designed to collect data on patients' health related quality of life scores. The measures used were:

- EQ-5D
- EORTC QLQ-C30
- EORTC QLQ-CLL 16
- Clinical Profile Form

The EQ-5D and the EORTC QLQ-C30 are standardised instruments to measure health outcomes. The EQ-5D has five dimensions: mobility, self-care, daily activities, pain and anxiety/depression. These dimensions are measured on a three level scale: no problems, some problems or extreme problems. The EORTC QLQ-C30 comprises five functional scales, a global measure of quality of life, three symptom scales and 6 single items. The five functional scales are: physical, role, cognitive, emotional and social functioning. The three symptom scales are: fatigue, pain and, nausea and vomiting. The six single item assess: Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrhoea and Financial Difficulties. The functional items are measured on a 4 point scale from not at all to very much. These scores are transformed to provide a rating from 0 – 100. For the functioning and global health measures high scores represent a high level of functioning and low scores represent severe difficulties in functioning. For the symptom scales and the single item scales high scores represent a high level of symptomatology or problems.

The EORTC QLQ-CLL 16 is a 16 item disease specific measure that comprises five domains of health related quality of life (HRQoL) important in CLL. There are three multi item scales: Fatigue (2 items), Treatment Side Effects (4 items) Disease Effects (4 items) Infection (4 items) and two single item scales on social activities and future health worries. These are measured on a four point scale where 1 = not at all and 4 = very much. These scores are transformed to give a rating from 0 – 100, where 0 = no symptoms or problems and 100 = a severe symptoms or problems.

Procedure

Using a Patient Enrolment Form eligible patients were identified. The inclusion and exclusion criteria can be found in Appendix 1. While attending an outpatient's appointment eligible patients were asked by their consultant whether they would take part in the study. The patients were given a patient information sheet and consent forms. After a 24 hour period, a site research nurse contact the patients by telephone, letter, or when the patient next attended the outpatients' clinic to ask them whether they had decided to take part in the study. Patients that consented were asked to return the signed consent forms. On receipt of the consent forms the site research nurse competed the Patient Information Sheet and arranged for the participants to complete the questionnaires.

At the request of NICE we have reported initial interim findings. The study is designed to recruit 250 patients in total.

Results

The participant demographic data can be found in Table 1a and Table 1b. In addition data are presented in terms of progression free survival and disease progression – the two main health states in the cost effectiveness model. The clinical profile of the sample is shown in Table 1c.

The utility values by total sample and by group are shown in Table 2. Table 3 displays the scores for the QLQ-C30 function scales (Global health status/ quality of life; Physical functioning; Emotional functioning; Cognitive functioning, and Social functioning). It also shows the scores for the QLQ-C30 symptom scales/ items (Fatigue; Nausea and vomiting; Pain; Dyspnoea; Insomnia; Appetite loss; Constipation; Diarrhoea and Financial Difficulties). The QLQ-C30 function scales scores range from 0 = (worst level of functioning) to 100 (best level of functioning). The QLQ-C30 symptom scales scores range from 0 = (no symptoms) to 100 (worst level of symptoms). The QLQ-CLL 16 scores range from 0 (no problems) to 100 (worst level of symptoms).

Conclusions & Limitations

These numbers may give an indication of findings of this study when it is completed. However we believe they should be interpreted with extreme caution. The sample size is too small for the results to be considered reliable. In addition there is a substantial variability between patients as would be expected and this makes interpreting the data very difficult.

Table 1a: Age characteristics of adult participants

	Progression free?					
	Total		PFS		Disease progression	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
AGE	65.20	9.78	65.00	10.88	66.00	5.66

Table 1b: Other sample characteristics

		Disease state					
		PFS		Disease progression		Total	
		Count	%	Count	%	Count	%
Sex	Male	7	87.5%	2	100.0%	9	90.0%
	Female	1	12.5%	0	.0%	1	10.0%
Ethnicity	Asian	0	.0%	0	.0%	0	.0%
	Black	0	.0%	1	50.0%	1	10.0%
	Chinese or other	0	.0%	0	.0%	0	.0%
	Mixed race	1	12.5%	0	.0%	1	10.0%
	White	7	87.5%	1	50.0%	8	80.0%
	Other	0	.0%	0	.0%	0	.0%
	Prefer not to answer	0	.0%	0	.0%	0	.0%
Education	No qualifications	2	25.0%	0	.0%	2	20.0%
	GCSE grades A - C	2	25.0%	0	.0%	2	20.0%
	Other	0	.0%	0	.0%	0	.0%
	Higher education	3	37.5%	1	50.0%	4	40.0%
	Degree or equivalent	1	12.5%	1	50.0%	2	20.0%
	Prefer not to answer	0	.0%	0	.0%	0	.0%
Employment	Full-time	3	37.5%	1	50.0%	4	40.0%
	Part time	0	.0%	0	.0%	0	.0%
	Homemaker	0	.0%	0	.0%	0	.0%
	Disabled	1	12.5%	0	.0%	1	10.0%
	Unemployed	0	.0%	0	.0%	0	.0%
	Retired	4	50.0%	1	50.0%	5	50.0%
	Prefer not to answer	0	.0%	0	.0%	0	.0%

Table 1c. The current and previous treatment for each responder category for progression free and disease progression participants

Patient ID	Response Category	Current treatment	Previous Treatment
Progression Free Participants			
101	Partial Responder	None	Fludarabine/Cyclophosphamide + Rituximab X 2 cycles Completed August 2008 Fludarabine/Cyclophosphamide + Rituximab X 2 cycles Completed Feb 2008 Fludarabine/Cyclophosphamide X 3 cycles Fludarabine/Cyclophosphamide X 6 cycles Completed 2005
107	Partial Responder	None	Chlorambucil/Rituximab x 6 cycles Completed Oct 2008
109	Partial Responder	None	Chorambucil Completed June 2008
103	Currently on Treatment	Chlorambucil/Rituximab x 4 Start Date July 2008	None
104	Currently on Treatment	Fludarabine/Cyclophosphamide + Rituximab x 2 cycles Start Date Oct 2008	Fludarabine/Cyclophosphamide x 4 cycles Completed Sept 2008
105	Currently on Treatment	Fludarabine/Cyclophosphamide 6 cycles Start Date June 2008 – Completed Nov 2008	Chlorambucil x 6 cycles Completed Aug 2007
108	Currently on Treatment	Fludarabine/Cyclophosphamide 6 cycles Start date May 2008	Chlorambucil/Rituximab Completed May 06 Rituximab x 4 cycles Completed 2004 Fludarabine Completed 2002
106	Complete Responder	None	Fludarabine/Cyclophosphamide Completed Oct 07
201	Stable Disease	None	Fludarabine/Cyclophosphamide Completed Nov 04
Disease Progression Participants			
102	Progressive Disease	Steroids started Jan.08 for an adverse event	Chlorambucil/Rituximab x 1 cycle Completed Dec 2007
202	Progressive Disease	None	Chlorambucil x 3 cycles Fludarabine/Cyclophosphamide No treatment dates

Table 2. Mean utility scores and descriptive statistics for participants by disease state

		Disease state		
		PFS	Disease progression	Total
EQ-5D utility	Mean	.77	.92	.80
	Median	.88	.92	.92
	Standard Deviation	.32	.11	.29
	Maximum	1.00	1.00	1.00
	Minimum	.09	.85	.09
	Missing	1	0	1

Table 3a Average Scores and indicators of dispersion for the QLQ-C30 Functional Scales & Global quality of life (100=High quality of life)

		Disease state		
		PFS	Disease progression	Total
Global Health Status / QoL	**Mean**	**75.00**	**75.00**	**75.00**
	Median	83.33	75.00	83.33
	Standard Deviation	27.32	11.79	24.72
	Maximum	100.00	83.33	100.00
	Minimum	25.00	66.67	25.00
	Missing	0	0	0
Physical Functioning	**Mean**	**87.04**	**90.00**	**87.58**
	Median	100.00	90.00	100.00
	Standard Deviation	21.11	14.14	19.44
	Maximum	100.00	100.00	100.00
	Minimum	50.00	80.00	50.00
	Missing	0	0	0
Role Functioning	**Mean**	**83.33**	**100.00**	**86.36**
	Median	100.00	100.00	100.00
	Standard Deviation	26.35	.00	24.52
	Maximum	100.00	100.00	100.00
	Minimum	33.33	100.00	33.33
	Missing	0	0	0
Emotional Function	**Mean**	**76.85**	**79.17**	**77.27**
	Median	91.67	79.17	91.67
	Standard Deviation	29.69	17.68	27.15
	Maximum	100.00	91.67	100.00
	Minimum	25.00	66.67	25.00
	Missing	0	0	0
Cognitive Function	**Mean**	**81.48**	**100.00**	**84.85**
	Median	83.33	100.00	83.33
	Standard Deviation	17.57	.00	17.41
	Maximum	100.00	100.00	100.00
	Minimum	50.00	100.00	50.00
	Missing	0	0	0

Social Function	**Mean**	**79.63**	**83.33**	**80.30**
	Median	100.00	83.33	100.00
	Standard Deviation	32.03	23.57	29.64
	Maximum	100.00	100.00	100.00
	Minimum	16.67	66.67	16.67
	Missing	0	0	0

Table 3b Average Scores and indicators of dispersion for the QLQ-C30 Symptom Scales/ items (0=no symptoms)

		Progression free?		
		PFS	Disease progression	Total
Fatigue	Mean	22.22	22.22	22.22
	Median	11.11	22.22	11.11
	Standard Deviation	29.40	15.71	26.76
	Maximum	77.78	33.33	77.78
	Minimum	.00	11.11	.00
	Missing	0	0	0
Nausea Vomiting	Mean	3.70	.00	3.03
	Median	.00	.00	.00
	Standard Deviation	7.35	.00	6.74
	Maximum	16.67	.00	16.67
	Minimum	.00	.00	.00
	Missing	0	0	0
Pain	Mean	9.26	16.67	10.61
	Median	.00	16.67	.00
	Standard Deviation	18.84	23.57	18.67
	Maximum	50.00	33.33	50.00
	Minimum	.00	.00	.00
	Missing	0	0	0
Dyspnoea	Mean	14.81	16.67	15.15
	Median	.00	16.67	.00
	Standard Deviation	29.40	23.57	27.34
	Maximum	66.67	33.33	66.67
	Minimum	.00	.00	.00
	Missing	0	0	0
Insomnia	Mean	37.04	.00	30.30
	Median	33.33	.00	33.33
	Standard Deviation	35.14	.00	34.82
	Maximum	100.00	.00	100.00
	Minimum	.00	.00	.00
	Missing	0	0	0

Appetite	Mean	7.41	.00	6.06
	Median	.00	.00	.00
	Standard Deviation	22.22	.00	20.10
	Maximum	66.67	.00	66.67
	Minimum	.00	.00	.00
	Missing	0	0	0
Constipation	Mean	11.11	.00	9.09
	Median	.00	.00	.00
	Standard Deviation	23.57	.00	21.56
	Maximum	66.67	.00	66.67
	Minimum	.00	.00	.00
	Missing	0	0	0
Diarrhoea	Mean	11.11	.00	9.09
	Median	.00	.00	.00
	Standard Deviation	23.57	.00	21.56
	Maximum	66.67	.00	66.67
	Minimum	.00	.00	.00
	Missing	0	0	0
Finance difficulties	Mean	25.93	16.67	24.24
	Median	.00	16.67	.00
	Standard Deviation	43.39	23.57	39.70
	Maximum	100.00	33.33	100.00
	Minimum	.00	.00	.00
	Missing	0	0	0

Table 4 HRQL data by disease state as measure by the EORTC CLL-16 (0=no problems)

		Disease state		
		PFS	Disease progression	Total
Fatigue	**Mean**	**20.37**	**16.67**	**19.70**
	Median	.00	16.67	.00
	Standard Deviation	33.10	23.57	30.57
	Minimum	.00	.00	.00
	Maximum	83.33	33.33	83.33
Treatment Side Effects	**Mean**	**14.81**	**29.17**	**17.42**
	Median	8.33	29.17	16.67
	Standard Deviation	18.99	17.68	18.80
	Minimum	.00	16.67	.00
	Maximum	50.00	41.67	50.00
Disease Effects	**Mean**	**14.81**	**12.50**	**14.39**
	Median	8.33	12.50	8.33
	Standard Deviation	21.15	17.68	19.75
	Minimum	.00	.00	.00
	Maximum	58.33	25.00	58.33
Infection	**Mean**	**16.67**	**20.83**	**17.42**
	Median	16.67	20.83	16.67
	Standard Deviation	13.82	29.46	15.57
	Minimum	.00	.00	.00
	Maximum	41.67	41.67	41.67
Social Problems	**Mean**	**14.81**	**.00**	**12.12**
	Median	.00	.00	.00
	Standard Deviation	24.22	.00	22.47
	Minimum	.00	.00	.00
	Maximum	66.67	.00	66.67
Future Health	**Mean**	**25.93**	**50.00**	**30.30**
	Median	.00	50.00	.00
	Standard Deviation	32.39	70.71	37.87
	Minimum	.00	.00	.00
	Maximum	66.67	100.00	100.00

APPENDIX 1

Inclusion Criteria (baseline assessment)

1. Patients with chronic lymphocytic leukaemia
2. Patients receiving first line therapy
3. Patients receiving 2nd line therapy. This will include patients who previously have responded well to first line therapy (relapse was >12 months after finishing the first line therapy) and are receiving the same therapy again
4. Within the past three months, patients whose treatment has been stopped after 2-3 cycles of 1st or 2nd line therapy and who have not yet received any further therapies
5. Patients receiving their 3rd, 4th , 5th or 6th cycle of 1st or 2nd line therapy
6. Patients who have completed therapy, are considered stable and are between 3 – 12 months post therapy
7. Life expectancy > 6 months
8. ECOG performance status 0-1
9. Patients aged ≥ 18
10. Willing and able to provide written informed consent

Exclusion Criteria (baseline assessment)

Any patient meeting one or more of the following exclusion criteria may <u>not</u> be entered into the study:

1. Has a clinically significant disorder (other than chronic lymphocytic leukaemia and chronic lymphocytic comorbidities) or any other condition, including alcohol or drug abuse, which may interfere with study participation or which may affect the conclusion of the study as judged by the investigator.
2. Has a mental disability or significant mental illness, legal incapacity or limited legal capacity or any other lack of fitness, in the investigator's opinion, to preclude the subject's participation in or ability to complete the study.
3. Patients will be excluded if in the opinion of the local investigator or research nurse they are currently experiencing a high degree of comorbid burden that might affect the accuracy of the quality of life data.