Chronic lymphocytic leukaemia treatment and outcome in the UK's population-based Haematological Malignancy Research Network

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Introduction

Few studies have evaluated the management and outcome of CLL in the general population. We investigated this using a specialist UK population-based registry, the Haematological Malignancy Research Network (www.hmrn.org).

Methods

Within HMRN, patient care is provided by 14 hospitals serving a population of ~4 million and all diagnoses across the region are made and coded by clinical specialists at a single integrated haematopathology laboratory – the Haematological Malignancy Diagnostic Service (www.hmds.info). All patients have prognostic, full-treatment, response and outcome data collected directly from medical records and notifications of deaths are supplied by the national Medical Research Information Service.

1,030 patients newly diagnosed 2005-9 were followed until 2014. Demographic, prognostic, treatment and outcome were analysed using standard statistical methods; relative survival was estimated using UK national life tables.

Results

With a median age of 71 years (range 26-97), 62% of patients were male, 88% had an ECOG score of 0-1, 15% had B-symptoms, 76% were Binet Stage A and 50% were in the low Rai group. With respect to initial treatment, 83% were managed by watch and wait for 6 months or more and 12% by chemotherapy (Table). The latter group were more likely to have B-symptoms (45%), advanced disease (Binet Stage C=44%, Rai High=51%) and be tested (79%) for a del(17p13) mutation; 25% of those tested had the deletion.

Table: Baseline patient characteristics by first line treatment

	Total n (%)	Age (years) Mean (SD)	Males %	ECOG 0-1 %	B symptoms %	Binet Stage %			Rai modified risk group %			del(17p13) %	
						A	B	C	Low	Intermediate	High	Tested	Deletion
Total	1030[1] (100)	70.6 (11.5)	61.7	87.8	14.9	76.4	10.0	12.1	49.8	30.7	17.3	31.1	17.2
Watch and Wait	853 (82.8)	70.1 (11.4)	60.6	91.5	11.0	83.9	7.6	7.0	56.9	29.6	11.5	23.7	12.9
Chemotherapy	121 (11.7)	69.0 (11.2)	71.9	86.8	45.3	21.7	31.1	44.3	2.8	42.5	50.9	79.3	25.0
Palliative / Supportive Only	55 (5.3)	81.2 (7.5)	58.2	31.4	15.7	70.6	3.9	25.5	35.3	23.5	41.2	38.2	23.8

[1]*One patient was treated with radiotherapy*

Median follow-up was 7 years and median survival was 8.1 years; 5-year overall survival was 64.1% increasing to 81.3% for relative survival, indicating that death was not solely attributable to CLL (Figure 1). Age was strongly predictive of outcome; 5-year overall survival (OS) estimates were 91% in those <60 years (n=190) and 25% in those 80+ years (n=225); corresponding 5-year relative survival (RS) estimates being 93% and 51% respectively (Figure 2). 5-year OS was 42% in those with a 17p13 deletion vs. 61% in patients with wild-type (Figure 3).

Figure 1: Overall and relative survival by first line treatment

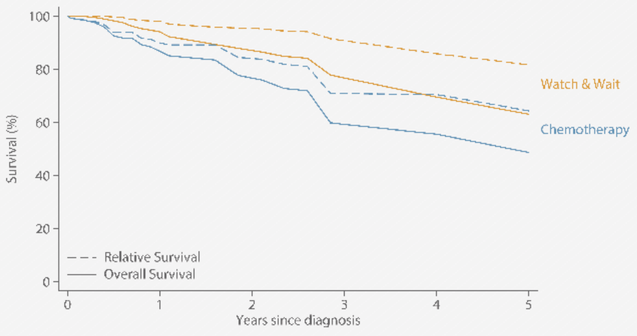


Figure 2: Overall and relative survival by age at diagnosis

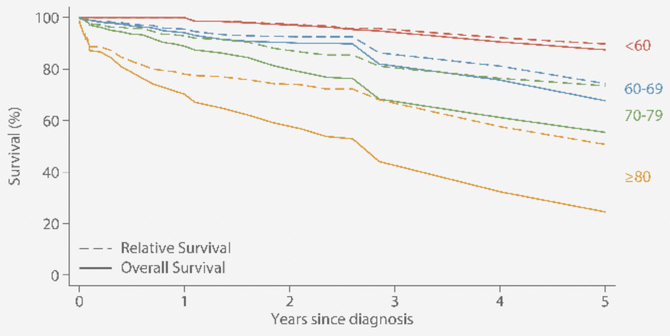
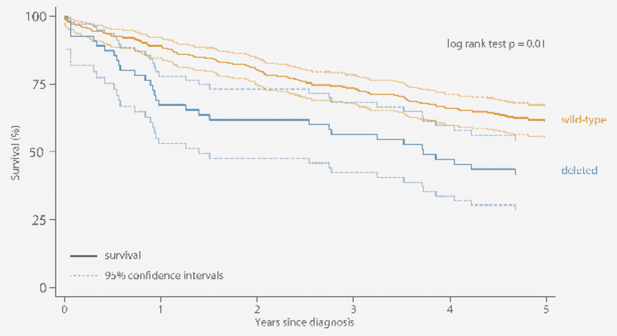


Figure 3: Overall survival by del(17p13) status



In total, 311 patients were treated with chemotherapy, 121 initially and 190 after a period of observation, on average, treatment started 2 years after diagnosis. Survival was examined from start of treatment and 5-year OS and RS estimates were 49% and 62% respectively. Survival was poorest for patients treated with chlorambucil, but this group on average was older (78 years) and not all of the deaths were not solely attributable to CLL; 5-year OS and RS being 27% and 40% respectively. By contrast, 5-year OS and RS for those treated intensively (FCR, FC and R-Chlorambucil) were more closely aligned (Figure 4).

Median progression-free survival in patients treated with chemotherapy was 2.9 years; was shortest for those treated with chlorambucil (1.5) and longest for FCR (4.4) (Figure 5). 95 (31%) of those treated with chemotherapy went on to receive second line therapy, either due to refractory disease or relapse; median survival from this point being 2.7 years. No variations by regimen were detected (Figure 6).

*Figure 4: Overall and relative survival by chemotherapy**

*Figure 5: Progression free survival by first line chemotherapy**

*Figure 6: Overall survival by second line chemotherapy**

**data not shown for regimens with less than 10 patients*

Conclusion

Analysis of data from our unselected UK population-based cohort demonstrate that, outside trials, survival from CLL is generally very good; with a 5-year RS > 80%. This is especially marked in younger patients, as well as those on watch and wait, where only 20% went on to chemotherapy. Older patients, generally treated with chlorambucil, had the worst survival; but amongst those treated more intensively no survival differences were detected by chemotherapy regimen.

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CLL

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