Social deprivation independently impacts clinical outcomes in patients with chronic lymphocytic leukemia

Authors

Gregory Fegan,[1] Daniel Tod,[1] Abigail Downing,[2] Nagah Elmusharaf,[2] Christopher Pepper[3] and Christopher Fegan[4]

[1]Swansea Trial Unit, Swansea University Medical School, Singleton Park, Swansea; [2]Department of Hematology, University Hospital of Wales, Heath Park, Cardiff; [3]Brighton and Sussex Medical School, University of Sussex, Brighton and [4]Institute of Cancer and Genetics, School of Medicine, Cardiff University, Heath Park, Cardiff, UK

Correspondence:
C. FEGAN - Fegancd1@cardiff.ac.uk

Supplementary Table 1 Hazard ratios for prognostic markers of overall survival

	Simple Model - 1 explanatory variable	Basic Multiple regression model	Basic model & LDT	Basic model & B2M	Basic model, B2M & Genetic	Basic model, B2M & Vh Status
Welsh Index of Multiple Deprivation (N=662)	Reference = Most Deprived Hazard Ratio (HR), [95% C.I of HR], P-value					
2nd Most Deprived	0.85 [0.59, 1.25] 0.413	0.80 [0.54, 1.18] 0.260	1.02 [0.63, 1.67] 0.924	1.07 [0.66, 1.75] 0.777	0.49 [0.23, 1.03] 0.058	0.81 [0.38, 1.73] 0.586
2nd Least Deprived	0.80 [0.52, 1.22] 0.294	0.68 [0.43, 1.07] 0.097	0.96 [0.57, 1.62] 0.875	0.67 [0.37, 1.20] 0.177	0.42 [0.18, 0.96] 0.039	0.39 [0.15, 1.01] 0.052
Least Deprived	0.59 [0.42, 0.82] 0.002	0.57 [0.40, 0.81] 0.002	0.75 [0.48, 1.17] 0.203	0.71 [0.45, 1.12] 0.141	0.37 [0.19, 0.73] 0.004	0.5 [0.25, 1.00] 0.05
Age Quartiles (N=662)	Reference = <55 Years HR, [95% C.I of HR], P-value					
55-64	1.42 [0.88, 2.31] 0.155	1.59 [0.95, 2.66] 0.076	1.55 [0.80, 3.03] 0.197	1.34 [0.75, 2.41] 0.321	1.38 [0.73, 2.59] 0.316	1.70 [0.76, 3.79] 0.193
65-74	2.15 [1.38, 3.34] 0.001	2.20 [1.37, 3.53] 0.001	2.83 [1.56, 5.14] 0.001	1.80 [1.05, 3.09] 0.034	1.79 [0.95, 3.37] 0.073	2.15 [1.05, 4.39] 0.035
≥75	6.34 [4.11, 9.78] <0.001	7.99 [4.96, 12.87] <0.001	9.02 [5.00, 16.26] <0.001	8.05 [4.60, 14.07] <0.001	9.90 [4.30, 22.78] <0.001	8.17 [3.08, 21.65] <0.001
Stage at diagnosis (N=661)	Reference = A or A0 HR, [95% C.I of HR], P-value					
B	1.96 [1.28, 3.00] 0.002	2.79 [1.75, 4.44] <0.001	4.37 [2.22, 8.60] <0.001	2.51 [1.48, 4.25] 0.001	2.00 [1.07, 3.75] 0.030	2.04 [0.95, 4.38] 0.068
C	2.59 [1.70, 3.93] <0.001	4.38 [2.79, 6.86] <0.001	2.64 [0.80, 8.70] 0.112	2.85 [1.62, 5.01] <0.001	3.36 [1.71, 6.60] <0.001	3.75 [1.53, 9.23] 0.004
CD38 status (N=591)	Reference = <20 % HR, [95% C.I of HR], P-value					
CD38 ≥20%	1.90[1.45, 2.49]<0.001	1.84[1.39, 2.42]<0.001	1.43[1.03, 2.00]0.033	2.03[1.43, 2.88]<0.001	1.86[1.11, 3.13]0.019	2.21[1.25, 3.91]0.006
LDT (N=560)	Reference >= 12 HR, [95% C.I of HR], P-value					
<12	2.08 [1.43, 3.01] <0.001		1.43 [0.94, 2.18] 0.090			
B2M (N=491)	Reference = < 3.5 HR, [95% C.I of HR], P-value					
≥3.5 mg/l	2.48 [1.81, 3.40] <0.001			2.05 [1.44, 2.94] <0.001	1.48 [0.90, 2.45] 0.126	1.55 [0.91, 2.64] 0.110
Adverse Cytogenetics (N=265)	Reference NOT (ATM and/or P53 deletions) HR, [95% C.I of HR], P-value					
ATM and/or P53 deletion	2.51 [1.62, 3.89] <0.001				1.81 [1.04, 3.18] 0.037	

IGVH Status (N=221)	Reference = <0.98 Hazard Ratio, [95% C.I of HR], P-value)				
≥0.98	2.24 [1.48, 3.41] <0.001				2.14 [1.19, 3.84] 0.011
Observations	590	505	439	224	160

Adverse cytogenetics = deletion of 11q and/or 17p.

Binet stage at diagnosis – Stage A0 No lymphadenopathy, Stage A Lymphadenopathy <3 sites,   Stage B – 3 or more lymphoid site enlargements, Stage C – Haemoglobin <10g/dl and/or Platelets <100 x109/l.

B2M – Beta2Microglobulin

LDT – Lymphocyte Doubling Time - <12 - ≥12 months

IGVH - Immunoglobulin Heavy-chain gene Variable region

Supplementary Table 2 Age at Diagnosis and Death

WIMD Quartiles	Age at Diagnosis								Age at Death							
	Overall Cohort		Subgroup: Stage A/A0 diagnosis		Subgroup: Stage B/C diagnosis		Mann-Whitney U Test (Stages A/A0 & B/C)		Overall Cohort		Subgroup: Stage A/A0 diagnosis		Subgroup: Stage B/C diagnosis		Mann-Whitney U Test (Stages A/A0 vs B/C)	
	Median age [p25, p75]	n	Median age [p25, p75]	n	Median age [p25, p75]	n			Median age [p25, p75]	n	Median age [p25, p75]	n	Median age [p25, p75]	n		
Most Deprived	65 [56, 74]	123	65 [57, 73]	102	67 [52, 77]	21	0.835		79 [67, 86]	58	79.5 [69, 86]	40	77.5 [61, 81]	18	0.102	
2nd Most Deprived	67 [57, 74]	137	68 [57, 76]	114	59 [51, 73]	23	0.041		80 [67, 86]	61	80 [67, 87]	47	70.5 [62, 81]	14	0.073	
2nd Least Deprived	65 [58, 75]	95	68 [58, 76]	83	61 [57.5, 64]	12	0.114		81.5 [69, 87]	42	82 [72, 88]	35	65 [63, 75]	7	0.003	
Least Deprived	67 [57, 75]	307	67 [58, 75]	278	57 [52.5, 65]	28	<0.001		80 [74, 87]	102	81 [77, 88]	87	72 [65, 75]	14	<0.001	
Overall Cohort	67 [57,74]	662	67 [58, 75]	577	60 [52, 69.5]	84	<0.001		80 [70, 86]	263	81 [74, 87]	209	71 [62, 79]	53	<0.001	
Mann-Whitney U Test (Most vs Least Deprived)	0.420		0.153		0.074				0.052		0.077		0.529			

WIMD = Welsh Index of Multiple Deprivation

Supplementary Table 3 Clinical therapeutic studies offered to patients

Clinical Trial n (%)	Most Deprived	2nd Most Deprived	2nd Least Deprived	Least Deprived	Total
No (not offered/entered a trial)	28 (22.76)	31 (22.63)	15 (15.79)	67 (21.82)	141 (21.3)
Yes (entered a trial)	13 (10.57)	18 (13.14)	12 (12.63)	34 (11.07)	77 (11.63)
Eligible but did not enter a trial as declined offer of a trial	2 (1.63)	3 (2.19)	2 (2.11)	3 (0.98)	10 (1.51)
Not Applicable	80 (65.04)	85 (62.04)	66 (69.47)	203 (66.12)	434 (65.56)
Total	123 (100)	137 (100)	95 (100)	307 (100)	662 (100)

Chi2(9) = 3.9117, P-value = 0.917