ELSEVIER

Blood 142 (2023) 6533–6535

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

642.CHRONIC LYMPHOCYTIC LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

Safety and Feasibility of a 16-Week Progressive Exercise Intervention in Treatment Naïve Chronic Lymphocytic Leukaemia

Frankie F Brown, PhD[1,2], Rebecca Oliver, BM BSc[1,3], Adam J Causer, PhD[1], Harrison D Collier-Bain, MSc,BSc[1], Annabelle Emery, PhD[1], Rachel Eddy[4], David Dutton[5], Josephine Crowe[3], Daniel Augustine[6,7], John Graby[6,1], Dan Rees[7], Daniela Rothschild Rodriguez[8], Oliver Peacock[7], Sally Moore[9], James Murray, MBBChir, PhD[3], James E Turner, PhD[1,10], John P Campbell, PhD[1]

[1] Clinical Rehabilitation and Exercise Medicine, Department for Health, University of Bath, Bath, United Kingdom
[2] School of Applied Sciences, Edinburgh Napier University, Edinburgh, United Kingdom
[3] Department of Haematology, Royal United Hospitals Bath NHS Foundation Trust, Bath, United Kingdom
[4] Department for Health, University of Bath, Bath, United Kingdom
[5] Department for Haematology, Great Western Hospitals NHS Foundation Trust, Swindon, United Kingdom
[6] Department for Cardiology, Royal United Hospitals Bath NHS Foundation Trust, United Kingdom, Bath, United Kingdom
[7] University of Bath, Bath, United Kingdom
[8] University of Southampton, Southampton, United Kingdom
[9] Department of Haematology, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, United Kingdom
[10] School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham, Birmingham, United Kingdom

A growing body of evidence from preclinical and human epidemiology studies of multiple cancer types indicate that physical activity can delay or avert the outgrowth of cancer, in a mechanistic process that may involve exercise-induced alterations to anti-cancer immunity. Many Chronic Lymphocytic leukaemia (CLL) patients present with asymptomatic, early-stage disease that is monitored until disease progression. Thus, exercise may be an effective way to manage disease burden and delay progression in treatment naïve CLL. The primary objective of this pilot study was to investigate the safety and feasibility of an exercise programme in people with treatment naïve CLL, and preliminarily explore the effects of exercise training on CLL counts, body composition, cardiorespiratory fitness, and immune cell phenotypes including T-cells.

We approached $N = 100$ treatment naïve CLL patients (Binet stage A and B) (Figure 1). Trial uptake was 40%, thus $n = 40$ participants with treatment naïve CLL were screened. After assessing suitability for exercise (e.g., resting electrocardiogram and other safety tests), $n = 11$ participants were excluded - the majority of these, $n = 9$, were due to the presence of cardiac abnormalities. Consequently, $n = 28$ participants were randomised into a 16-week, home-based, supervised, personalised, progressive exercise intervention ($n = 14$: mean ± SD: age = 62 ± 12 years) or 16-weeks of usual care, control group ($n = 14$: mean ± SD: age = 61 ± 10 years). The overall retention rate was 86%, with 79% of the exercise group and 93% of the control group completing the trial. Adherence to the exercise intervention was 92 ± 8%. One serious adverse event was reported (hospitalisation for pneumonia) that was unrelated to the trial and one adverse event was reported (syncope following exercise) that was related to the trial. Together, this evidence indicates that exercise training is both safe and feasible in people with treatment naïve CLL who passed pre-trial screening.

The exercise intervention elicited a 2% increase in DEXA-derived lean mass in the exercise group compared to a 0.4% decrease in the control group ($p = .01$) (Table 1). DEXA-derived total body fat percentage decreased by 4% and 1% and fat mass decreased by 3% and 2% ($p < .05$) respectively in the exercise and control groups but there was no significant difference between the groups ($p > 0.05$). Resting systolic and diastolic blood pressure was lower at post-intervention in both groups ($p < .05$); the exercise group reduced systolic and diastolic blood pressure by 5% and 2% respectively and the control group reduced by 6% and 7% respectively, but there was no significant difference between groups ($p>0.05$) suggesting the observed changes could be the result of "white coat hypertension" pre-intervention. Additionally, no changes were observed for whole-body mass, BMI, bone mineral density, resting heart rate, or measures of cardiorespiratory fitness (all $p>0.05$).

This trial provided a unique opportunity to investigate the effects of regular exercise on neoplastic activity in humans (i.e., CLL counts) without the confounding presence of anti-cancer therapy. Resting blood samples collected pre- and post-intervention were analysed by flow cytometry to enumerate $CD5^{+}CD19^{+}$ CLL cells clonally restricted to kappa or lambda. No differences

were observed for clonal CLL cells over time or between conditions ($p>0.05$) (Table 1). We also analysed resting blood samples collected pre- and post-intervention by flow cytometry to enumerate T cell subsets. No statistically significant changes were observed between conditions pre-intervention to post-intervention for $CD4^+$ or $CD8^+$ T-cell subsets including, naïve ($CD27^+CD45RA^+$), stem cell-like memory ($CD27^+CD45RA^+CD127^+CD95^+$), central memory ($CD27^+CD45RA^-$), effector memory ($CD27^-CD45RA^-$), EMRAs ($CD27^-CD45RA^+$) or exhausted T-cells ($PD1^+$, $Tim3^+$) or FoxP3 T-regulatory cells ($CD4^+CD127^{low}CD25^+FoxP3^+$) (all $p>0.05$).

Our results show that exercise is safe and feasible in people with treatment naïve CLL who passed pre-trial screening. In addition, exercise training increased lean mass. No changes were observed to CLL cells. The latter finding is unsurprising given the poorly immunogenic profile of CLL.

Disclosures No relevant conflicts of interest to declare.

https://doi.org/10.1182/blood-2023-186956

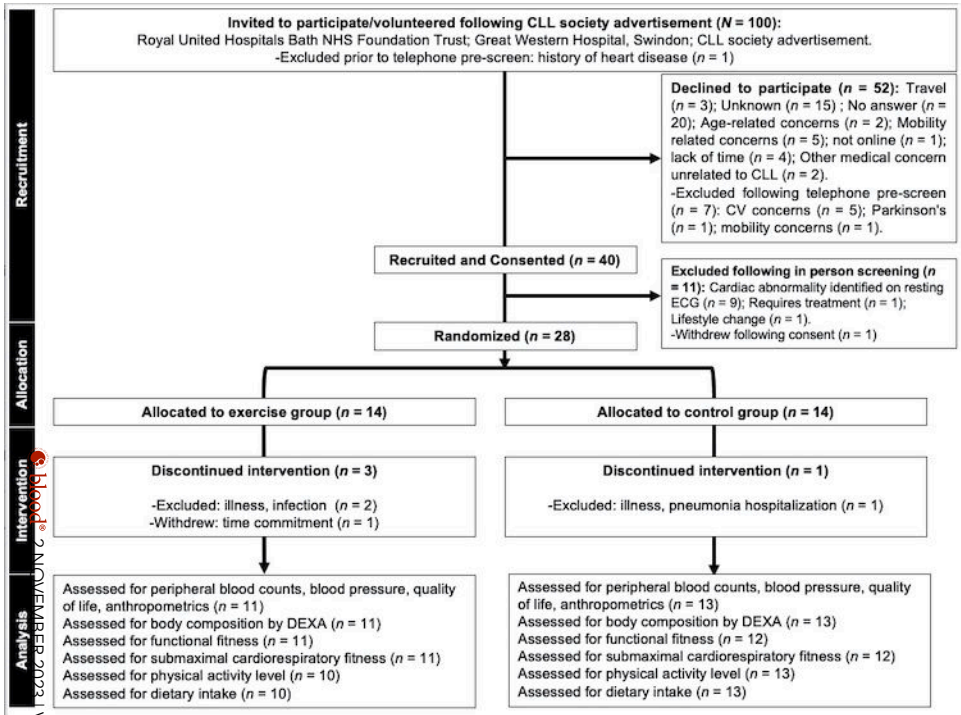

Table 1. Intervention related changes to body composition, resting CLL counts and cardiovascular measurements and cardiorespiratory fitness. Interaction and main effects from two-way repeated measures ANOVA are reported. Data are mean ± SD.

	Exercise		Control		Analysis		
Variable	Pre-Intervention	Post-Intervention	Pre-Intervention	Post-Intervention	Interaction (time x group)	Main effect time	Main effect group
Body composition							
Body mass (kg)	72.5 ± 17.4	72.7 ± 18.4	82.6 ± 17.5	81.7 ± 16.5	$p = .16, \eta2 = .09$	$p = .31, \eta2 = .05$	$p = .20, \eta2 = .08$
Body mass index (kg/m^2)	25.4 ± 5.2	25.5 ± 5.6	28.3 ± 4.8	28.1 ± 4.7	$p = .19, \eta2 = .08$	$p = .59, \eta2 = .01$	$p = .20, \eta2 = .07$
Body fat percentage (%)	33.5 ± 7.6	32.1 ± 7.4††	35.0 ± 8.7	34.5 ± 8.5††	$p = .15, \eta2 = .09$	$p = .004, \eta2 = .33$	$p = .56, \eta2 = .02$
Fat mass (kg)	24.5 ± 8.8	23.7 ± 9.0†	29.2 ± 10.4	28.5 ± 9.9†	$p = .83, \eta2 = .002$	$p = .03, \eta2 = .21$	$p = .24, \eta2 = .06$
Lean soft-tissue mass (kg)	48.0 ± 11.5	49.0 ± 11.9*	53.4 ± 12	53.2 ± 11.3*	$p = .01, \eta2 = .28$	$p = .07, \eta2 = .14$	$p = .33, \eta2 = .04$
Bone mineral density (g/cm^2)	1.14 ± 0.14	1.14 ± 0.16	1.24 ± 0.14	1.22 ± 0.13	$p = .09, \eta2 = .12$	$p = .11, \eta2 = .12$	$p = .11, \eta2 = .11$
CLL cells							
CD5$^+$CD19$^+$ kappa/lambda (cells/μL)	28,795 ± 21,071	25,375 ± 18,156	35,477 ± 57,005	35,734 ± 50,815	$p = .52, \eta2 = .02$	$p = .58, \eta2 = .01$	$p = .62, \eta2 = .01$
Cardiorespiratory fitness and resting cardiovascular measures							
Anaerobic threshold (O_2 mL·kg^{-1}·min^{-1})	14.2 ± 2.3	14.1 ± 2.3	13.2 ± 3.5	12.7 ± 4.7	$p = .65, \eta2 = .01$	$p = .43, \eta2 = .03$	$p = .36, \eta2 = .04$
Power at anaerobic threshold (W)	58.5 ± 12.5	62.5 ± 11.7	60.5 ± 24.1	61.8 ± 25.7	$p = .33, \eta2 = .05$	$p = .06, \eta2 = .16$	$p = .94, \eta2 = .00$
Resting systolic blood pressure (mmHg)	135.6 ± 19.1	129.3 ± 15†	138.0 ± 11.9	130.2 ± 15.1†	$p = .78, \eta2 = .004$	$p = .01, \eta2 = .25$	$p = .78, \eta2 = .004$
Resting diastolic blood pressure (mmHg)	83.5 ± 9.1	81.6 ± 6.3†	86.8 ± 5.3	80.4 ± 7.3†	$p = .14, \eta2 = .10$	$p = .01, \eta2 = .25$	$p = .67, \eta2 = .01$
Resting heart rate (beats/min)	65.4 ± 11.8	63.6 ± 11.8	61.7 ± 7.6	60.9 ± 6.5	$p = .65, \eta2 = .01$	$p = .24, \eta2 = .06$	$p = .41, \eta2 = .03$

*indicates significant interaction between time and group, suggesting the difference from pre-intervention is different between groups at $p < 0.05$, †indicates significant main effect of time, suggesting there is a difference from pre-intervention in both groups, but no difference between groups at $p < 0.05$, ††indicates significant main effect of time, suggesting there is a difference from pre-intervention in both groups, but no difference between groups at $p < 0.01$. The anaerobic threshold test is a submaximal exercise test used to measure cardiovascular fitness and anaerobic threshold is presented as millilitres of oxygen uptake per kilogram per minute, and separately as the power in watts at which the anaerobic threshold was achieved. ANOVA, analysis of variance; CLL, chronic lymphocytic leukaemia. Degrees of freedom were F(1,22) in all except the cardiorespiratory variables which were F(1,22) due to missing data from $n = 1$ control participant that did not complete the anaerobic threshold test post-intervention, therefore the pre-intervention was removed from the analysis. And only complete datasets were analysed.

Figure 1