DfE Project title: SPIN: a Study of Prehabilitation In Non-small cell lung cancer

Gillian Prue, Olinda Santin (Clinical link Dr Gerard Walls, CCRCB and NI Cancer Centre)

Aims and purpose of proposed investigation

To perform a single centre single group feasibility study of pre-habilitation high-intensity interval training (HIIT) and behavioural support to reduce symptom burden in NSCLC.

Objectives:

- To assess the feasibility and acceptability of delivering HIIT to non-small cell lung cancer (NSCLC) patients.
- To determine eligibility, recruitment and retention rates.
- To measure changes in patient-reported outcome measures for relevant symptoms (to include fatigue and breathlessness) and general health
- To assess changes in objective measures of fitness
- To correlate any change in symptom burden and fitness measures with clinical outcomes and treatment complications.
- To determine the rate of adverse events.
- To test intervention fidelity according to study protocol.
- To assess the extent to which intervention can be integrated into clinical practice.
- To collect preliminary data on health-related quality of life and health resource usage.
- To provide data for sample size calculation for a large scale UK wide RCT.

Background of the project

Many exercise oncology trials use a continuous moderate intensity approach to training (including those in lung cancer), but there has been a suggestion that non-linear training (i.e. interval training) traditionally used for athletes could be applied to cancer patients[1]. Through this project we hope to refine and determine the feasibility of this innovative approach, with a view to optimising exercise training in NSCLC and maximising the impact on symptom burden and possibly treatment response. Patients who do not reach a distance of 500 m during the 6-min walk test (6MWT) or a VO_2 max of less than 16 mL/kg per minute have an increased risk of postoperative complications and prolonged hospital stay[2,3]. There is some evidence of the effectiveness of pre-operative exercise on improving exercise capacity, post-operative complications[4] and fatigue, but current evidence is not sufficient to demonstrate the ideal type or intensity[5,6]. The effect of exercise on breathlessness in NSCLC has yet to be investigated[5]. HIIT is designed to minimise the duration of exercise sessions focussing on short bouts of high intensity exercise which may be more appropriate for lung cancer patients due to their short time to breathlessness[7]. Pre-operative HIIT has only been investigated in one underpowered Swedish study which did not examine the effect on patient symptoms[8] but did show improvements in fitness.

Plan of investigation and methodology

Study design: Single centre, single group feasibility study.

Target population: Proven or suspected NSCLC, stages I to III, being considered for curative intent therapy.

Inclusion criteria: 1.) pathologically proven or suspected NSCLC or clinical lung cancer as per the assessment of the Multi-Disciplinary Team (MDT); 2.) no evidence of metastatic disease on staging investigations at entry; 3.) deemed medically fit by treating team to participate in exercise programme; 4.) able to provide informed consent.

Exclusion criteria: 1.) comorbidity precluding participation in HIIT; 3.) pathologically proven small cell lung cancer; 4.) MRC dyspnoea score of 3 or poorer.

Sample size: a power calculation is not appropriate as the study does not aim to provide a definitive estimate of treatment effect. Rather the aim is to provide likely rates of recruitment

and retention, and to provide an estimate of the intervention impact to inform the definitive trial.

Intervention:

Exercise component: Adapted from that delivered by Licker et al.[8]: supervised HIIT cycling (cycle ergometer) (two 10 minute series of 15-second sprint intervals, interspersed by 15 second pauses and a 4 minute rest between the two series). Resistance exercise (body weight, resistance band and/or static weight machines) will be individually prescribed and tailored. Delivered two/three times per week prior to commencing treatment.

Behavioural support component: Based on The Theory of Planned Behaviour the overarching focus of the behavioural support will be to increase/enhance perceived control in task-specific exercises and overcoming individual barriers to exercise. The behavioural support provided will be encompassing, consistently delivered, and provided to each participant throughout the pre-habilitation programme.

Outcomes (assessed at baseline, immediately pre-treatment, and at 90 days post-treatment):

Primary outcomes: Fatigue (FACT-F) and breathlessness (MRC dyspnoea score).

Secondary:

1) Exercise capacity (predicted VO_2max, 6MWT)
2) Clinical outcomes (e.g. length of hospital stay, presence of grade toxicities e.g. dyspnoea and post-operative complications, 90-day mortality rate)
3) Health-related quality of life and impact on health resource use and work and activities using the following measures: EQ-5D-5L; a Health Resource Use questionnaire and a Work and Activities Questionnaire
4) Feasibility: percentage of participants completing baseline testing, intervention and follow-up testing, attendance rates and safety (number of adverse events). Semi-structured interviews conducted with participants, non-participants and health care professionals will explore perceived facilitators and barriers to exercise.

Analysis: Data on patient eligibility, recruitment and attrition rates (surgical and non-surgical) will be gathered. Compliance to the intervention will be analysed using descriptive analysis (as well as any exercise completed outside of the intervention). Thematic analysis will be used to identify themes within the information gained from qualitative interviews. Quantitative data will be analysed for mean change using repeated measures ANOVA.

Define the expected value of the research to the academic community and lung cancer patients

Lung cancer patients experience significant symptom burden as a result of the disease itself, pre-existing comorbidities and compounded by the side effects of treatment. The symptom burden is higher than that reported by other cancer diagnoses[10], with functional problems, severe dyspnoea and fatigue being the most distressing[11]. Our intervention has been designed to reduce this symptom burden.

If this study demonstrates that it is feasible for this patient group to participate in a pre-habilitation HIIT programme then an evaluation of such an intervention is warranted in a larger group to determine the effectiveness in improving symptom burden and outcomes.