Rigshospitalet

Centre for Cancer and Organ Diseases

Section of Palliative Medicine

Direct 35459692

Abstract

"Bridging molecular and patient-centered research in cancer cachexia: a translational protocol"

Date: 22 September 2021

Cachexia is a common adverse effect of cancer, and is associated with impaired physical function, reduced tolerance to anticancer therapy and reduced survival. Insulin resistance may play a key role in cancer cachexia (CC), likely due to insulins important anabolic effects on skeletal muscle. Exercise potently improves health by increasing strength, muscle protein synthesis, mitochondrial function, and insulin sensitivity in healthy humans and could presumably counteract CC development. Rodent data indicates an important role of the mitochondrion in the CC development, but translational research in this field is lacking.

The study population (N=80) will be newly diagnosed patients with non-small cell lung cancer (NSCLC) stage III/IV. Patients will be assessed before 1st and after the 4th cycle of treatment. Assessments include muscle function, registration of disease outcomes and treatment-related toxicity. Use of PROMs will provide detailed data on activity level, nutritional status and symptom burden, CC specific symptoms, quality of life and caregiver burden (WP1).

In a subgroup (n=40) muscle and adipose tissue (AT) biopsies will be taken before and after 4 cycles of treatment (WP2).

In addition, a subgroup of patients (n=24) will then undertake a 4-week one-leg-training program (WP3).

In Figure 1 an overview of work packages (WPs) is showed.

Three specific aims will be addressed in corresponding work packages (WPs):

1. **elucidate** the involvement of insulin resistance and **quantify** metabolic dysregulation in patients with NSCLC and **describe** the physical performance and body composition across 1st line treatment and **identify** possible predictive factors for disease outcomes and patient- and informal caregiver- reported outcomes (WP1).
2. **identify** molecular changes in skeletal muscle, adipose tissue (AT), and peripheral blood samples across 1st line NSCLC treatment, to establish possible predictive factors for muscle mass loss, fat browning, disease outcomes, and patient-reported outcomes (WP2).
3. **determine** global scale molecular and morphological changes of skeletal muscle tissue in response to exercise training (ET) and **establish** whether ET might reverse insulin resistance and improve metabolic regulation and muscle function and identify potential molecular mechanisms in patients with NSCLC-associated muscle dysfunction (WP3).

By bridging basic molecular and patient-centered research this translational project seeks a more mechanistic understanding of CC, the role of insulin resistance and the role of exercise and a better understanding of its implications for the patients and informal caregivers.

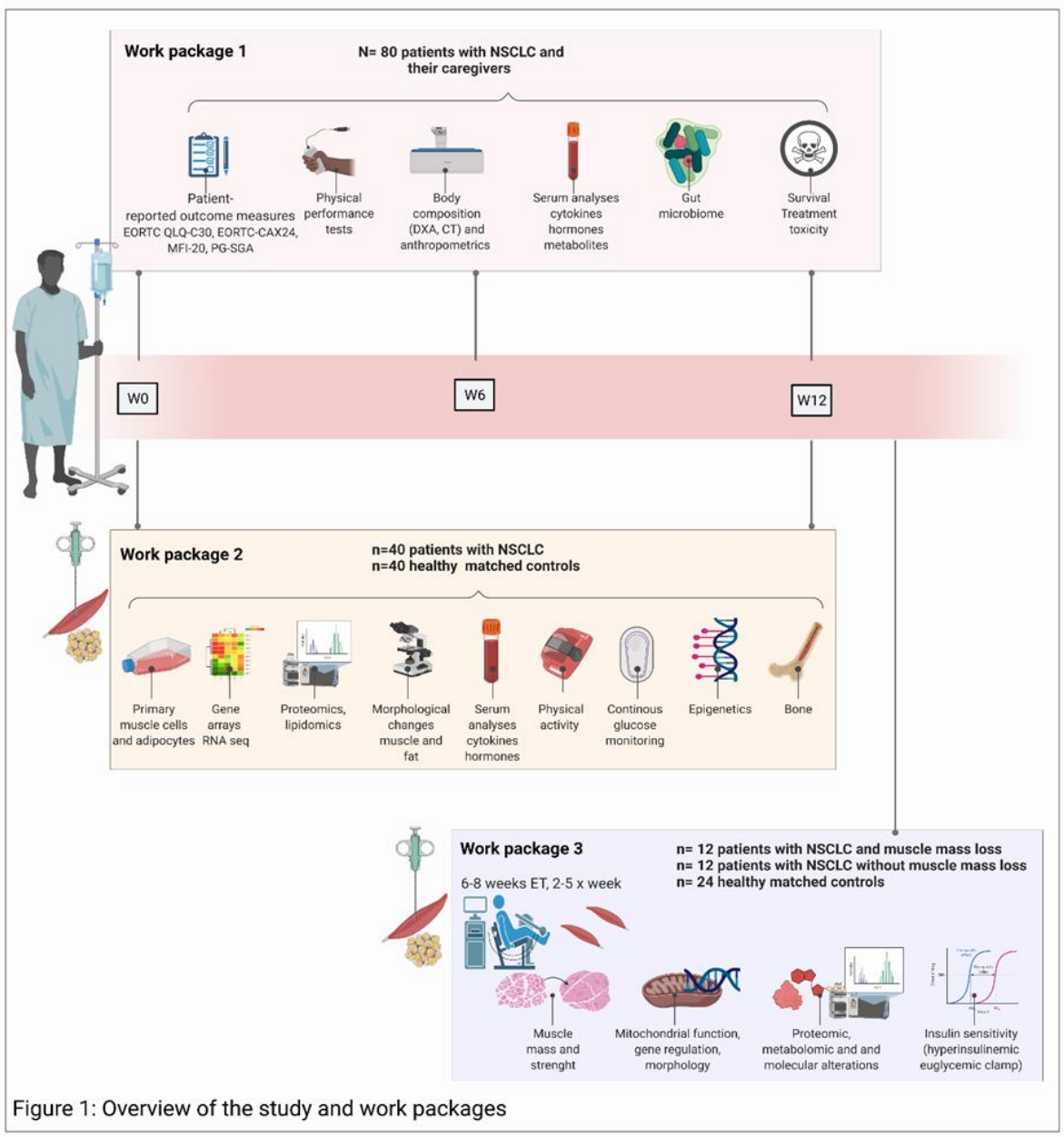

Figure 1: Overview of the study and work packages

Sponsor and primary investigator

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