

Animal vs vegetable protein supplementation during neoadjuvant chemotherapy in patients with gastrointestinal (GI) cancer: an

exploratory study

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Description of the initiative

• Background / context

The Mammalian Target of Rapamycin (mTOR) signalling pathway plays an essential role in cell growth and proliferation, whereas aberrant activation of mTOR has been linked to cancer cell proliferation in different cancer types.

• Rationale for the initiative

Milk proteins, namely casein, are rich sources of essential and branched chain amino acids, utilized in commercially available supplements in order to improve protein synthesis in patients at risk of malnutrition. However, they have also been shown to stimulate mTOR pathway, thereby raising concerns about promoting tumour growth in cancer patients. Thus, the most adequate protein type, which fulfills patient's nutritional requirements, but with minimal hypothesis of stimulating mTOR pathway, is still not defined.

• Objectives and scope

To analyze the effect of supplementing patients with GI cancer undergoing neo-adjuvant chemotherapy with animal or vegetable protein as compared to a control group. We will measure changes in nutritional status/ body composition, treatment response and toxicity as well as insulin growth factor 1 (IGF1), insulin and glucose levels which are known to activate mTOR.

Planned activities & deliverables

• Outline the steps to be taken

An open label randomized controlled trial (RCT) will be conducted to compare a control group with 2 intervention groups supplemented either with whey (animal) or pea (vegetable) protein on equal amounts. Calorie intake goal will be set at 30kcal/kg, protein intake at 1.5g/kg and monounsaturated fat at 30% of total energy intake. Insulin resistance will be analysed with the homeostasis model assessment (HOMA) and the glucose oral test. Tumour mTOR activity will be analysed by immunohistochemistry using p-p70S6k monoclonal antibody on tumour specimens obtained both pre-chemotherapy and post-operatively. We will also explore the influence of the intervention on patients' nutritional status, body composition and quality of life, treatment response and toxicity.

• What are the concrete deliverables of the project

Increase the knowledge about protein supplementation in cancer patients in whom we want to preserve nutritional status, minimize toxicity and maximize tumour response without stimulating tumour growth. Awareness of the role of type of protein intake on modulation of mTOR activity and response to chemotherapy.

What achievements are possible in the next 12 and 24 months?

0-12 months: preliminary data report, 12-24 months- Full report.

Resources & enablers

• Describe personnel, financial needs

Patients will be randomized to a control group (standard procedure), G1 (whey protein), G2 (pea protein). We need to pay 10% salary of a research dietitian (2 years); protein supplements for the 2 intervention groups during a 3 month period – neo-adjuvant chemotherapy.

CT scans are routinely performed for cancer staging and will be used to measure body composition. We need to buy a hand-grip dynamometer.

• Specify how the grant will be spent

Research dietitian: 4.000€; Pea protein supplements (35g/day, 1kg- 18 €, each patient with supplementation for 3 months-54 €, 30 patients-1620 €; whey protein supplements 30g/day, 1kg-20€, each patient with supplementation for 3 months-60€, 30 patients-1800€.

Plasma level of insulin, IGF1, glucose, glucose oral test will be performed in the Hospital facilities and mTOR antibody (250€ - each patient, 90 patients-)

What factors will make it successful?

Both the Oncology and the Surgery Departments of our Hospital are actively investing in reducing treatment complications and improving disease outcome. ERAS was implemented in our Hospital 2 yrs ago. We are a National reference Center for GI cancer. We treat approximately 100 patients / year with gastric and pancreatic cancer. Measuring body composition using a software that runs on Matlab is available at our Hospital. PROMs (including QoL questionnaires) are being implemented in our Hospital since 2017.

Results/outcomes & expected impact

• How will the findings be implemented?

We will be able to improve nutritional recommendations concerning type of protein. Scientific societies will be involved.

• How will this project advance patient care / contribute to optimal nutritional care?

GI cancer patients have a high prevalence of nutritional problems, namely sarcopenia which has been shown to influence short and long term survival, as well as quality of life. Protein suppl

What makes the project innovative?

Protein supplementation is recommended but type of protein namely whey protein as opposed to vegetable has been scarcely studied.

Will the project be likely to influence national nutrition policy?

Dietary counselling to cancer patients is not routine in all Portuguese Hospitals. If we demonstrate that type of protein influences final outcome in this population, it will be considered for routine treatment, supported by local and national guidelines.

Is the project transferable to other settings / countries?

If positive results can be demonstrated, findings from this study will certainly be used in other national and international Oncology centres.