



PRC

MultiAnam – Multimodal treatment including anamorelin in patients suffering from cancer cachexia

A proposed randomized controlled trial

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Disclosures

No personal conflicts of interest

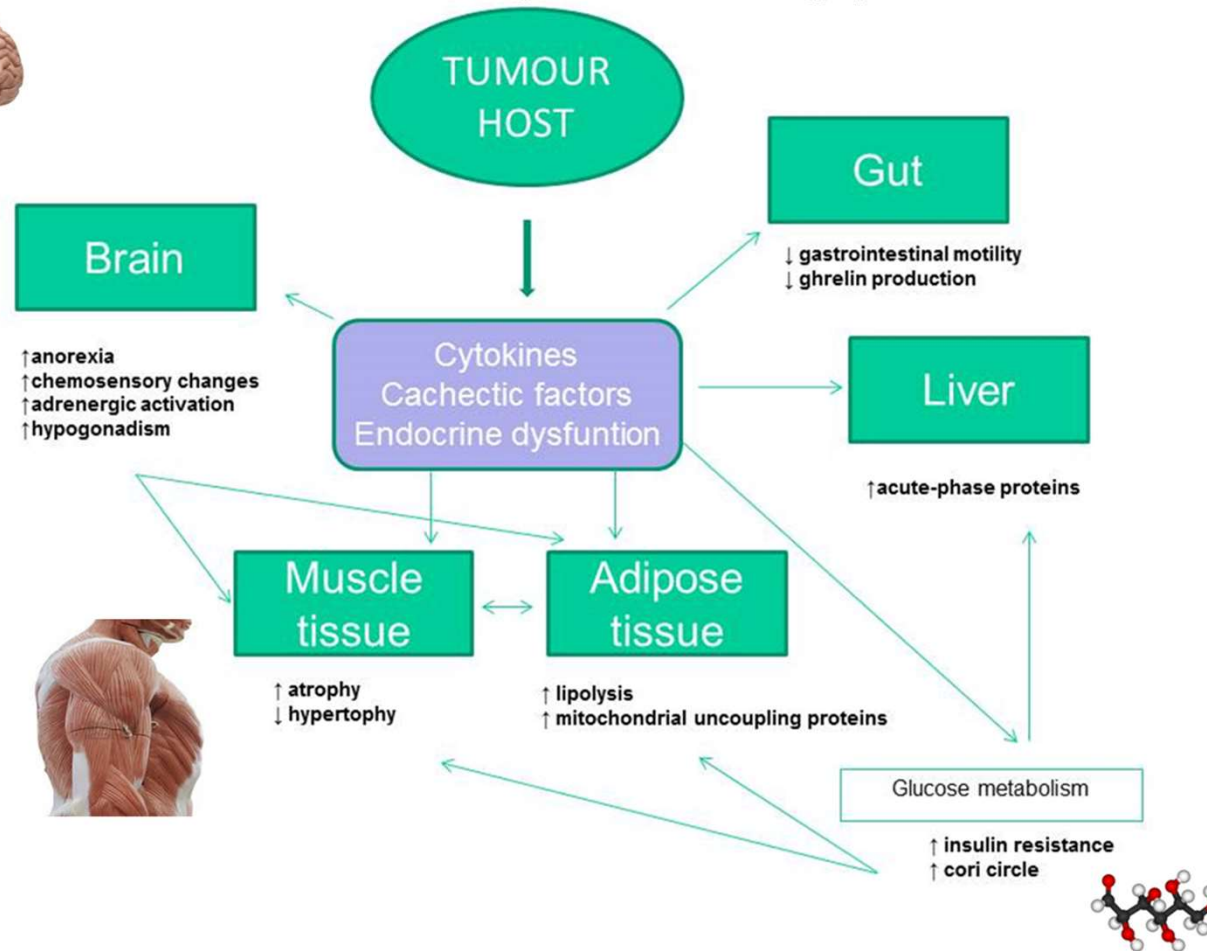
- Helsinn has agreed to supply the study drug free of charge

Cancer cachexia

- A multifactorial syndrome characterized by muscle loss (with or without fat loss) leading to impaired physical function
- Often reduced appetite/food intake
- Currently no treatment or standard of care



Cachexia pathophysiology



Multimodal interventions

Pathophysiology

Alterations in metabolism

Reduced food intake
Reduced physical activity

Cancer disease
Symptoms/side effects

Intervention

Anti-inflammatory
Anabolic
Appetite stimulating
etc

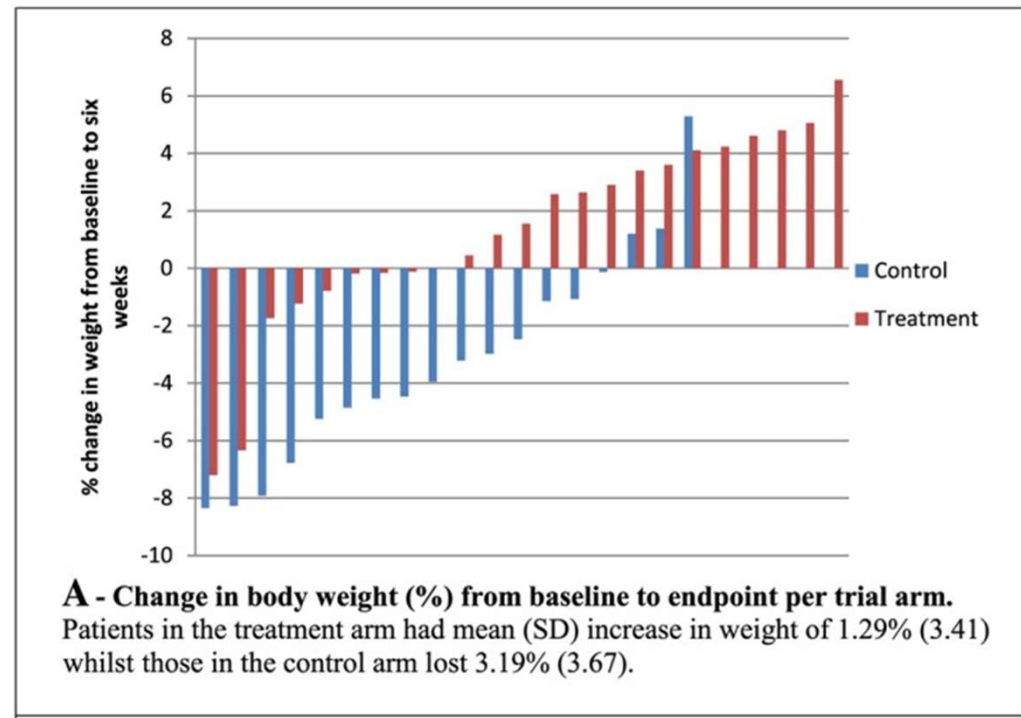
Sufficient nutrition
Physical exercise

Cancer treatment
Symptom treatment

Courtesy of T. Solheim

Pre-MENAC

- 46 patients with NSCLC or pancreatic cancer receiving chemotherapy
- 6-w multimodal intervention (including NSAID) vs. standard care
- Feasible and safe
- Promising results in terms of improving body weight



Solheim et al. J Cachexia Sarcopenia Muscle 2017



Anamorelin,
(synthetic ghrelin)

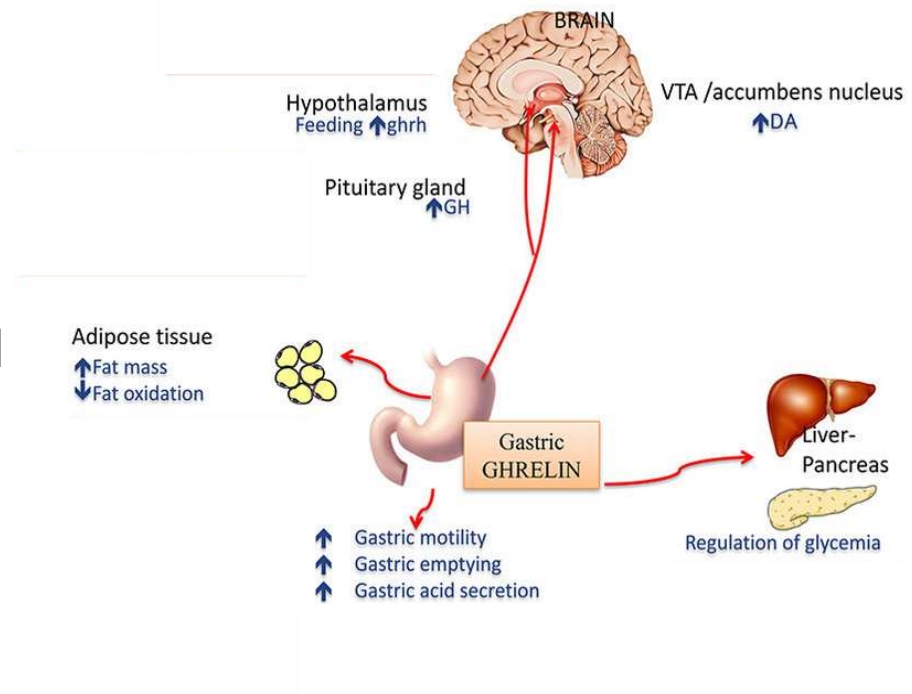
ONS w/Ω-3 FA
Physical exercise
programme

Cancer treatment
Symptom
treatment

- NSAID not an option for everyone
 - Renal failure
 - Asthma/COPD
 - Peptic ulcers
- Anamorelin
 - A synthetic ghrelin receptor agonist

Ghrelin – «hunger hormone»

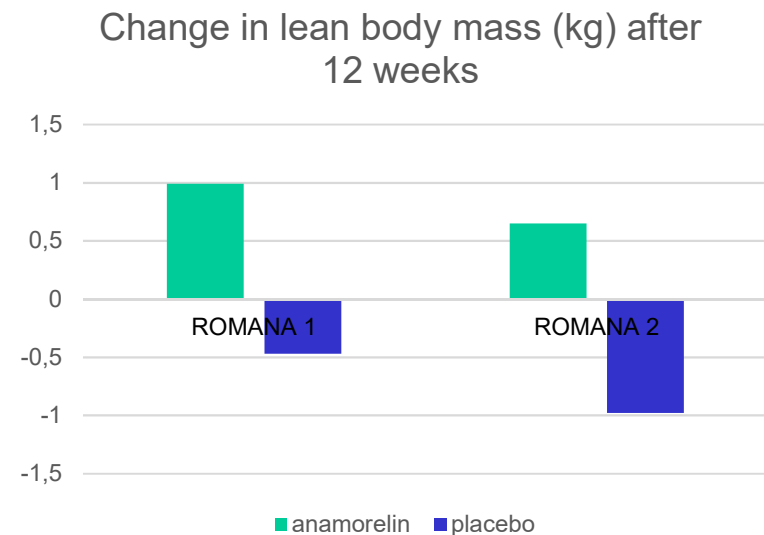
- A hormone released from the stomach
- Stimulates the pituitary and the hypothalamus
- Leads to increased appetite and secretion of growth hormone (anabolic potential)



Adapted from Gorwood et al. Front Neurosci 2016

Anamorelin

- ROMANA 1 & 2:
 - NSCLC and weight loss
 - Increase in lean body mass
 - No difference in hand grip strength
- Not received license
- Only tested as a single modality treatment



Temel et al. Lancet Oncol 2016

Objective

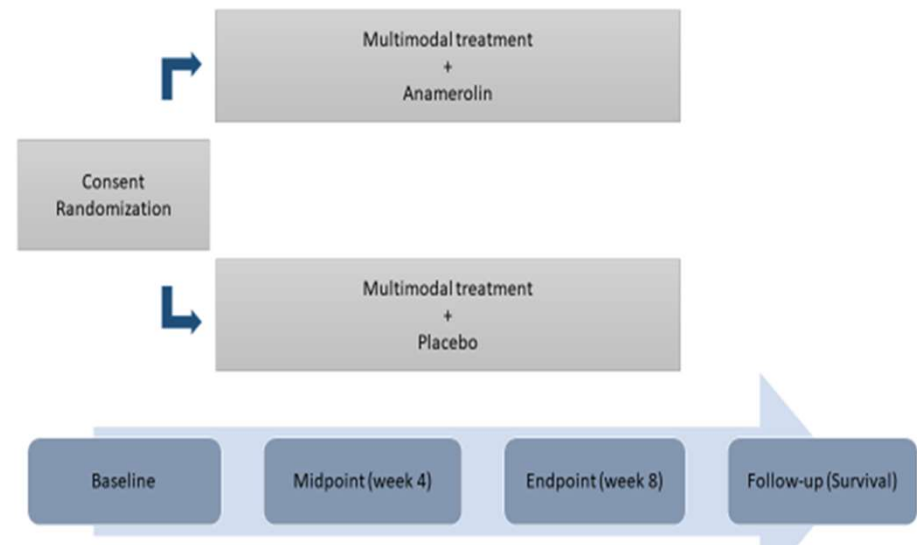
- To evaluate efficacy of anamorelin as part of a multimodal cachexia intervention in terms of improving body weight (primary) and physical performance (secondary) in patients with inoperable pancreatic cancer
 - Nutritional counselling
 - Oral nutritional supplements w/ Ω -3 fatty acids
 - Physical exercise program
 - Anamorelin or placebo

Patients

- Key inclusion criteria:
 - Primarily inoperable pancreatic adenocarcinoma, and no surgery planned in the intervention period (in case of neo-adjuvant chemotherapy)
 - Self-reported weight loss > 5% last six months
 - Karnofsky performance status > 70
 - Life expectancy at least 3 months
 - ≥18 years of age
 - Adequate hepatic and renal function
- Key exclusion criteria:
 - Patients with known brain metastases
 - Uncontrolled diabetes
- Estimated number of patients needed is 134

Design

- Randomized, double blinded, placebo controlled trial
- Both arms:
 - Nutritional counselling
 - Oral nutritional supplements w/ Ω -3 fatty acids
 - Physical exercise program
- Intervention/control arm
 - Anamorelin/Placebo



Treatment

- Nutrition
 - Nutritional counseling
 - 2 units of Ω -3-containing ONS, Supportan (Fresenius)
 - Alt. other ONS and Ω -3-capsules if Supportan is not tolerated
- Exercise program
 - 5 sessions with light aerobic exercise per week
 - 3 sessions of resistance training per week
- Anamorelin 100 mg daily or Placebo
- Chemotherapy and/or supportive/palliative treatment according to treating physician's discretion

Outcomes

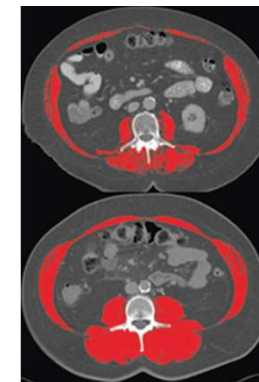
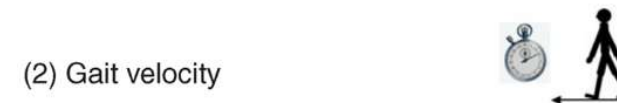
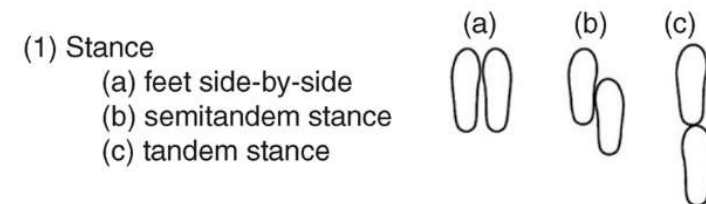
- Primary
 - Body weight (kg)
 - Key characteristic of cachexia
 - Easy to measure in clinical practice
 - Understandable and relevant to patients and clinicians
 - Sensitive to both loss of muscle and fat mass



Outcomes

- Secondary
 - Physical performance (SPPB)
 - Muscle mass (CT L3)
- Exploratory
 - PROMs
 - Health economy
 - Tolerance of cancer treatment
 - ...

Short Physical Performance Battery (SPPB):



Present status

- In its late stages of planning
- Four centres has agreed to participate
- Helsinn has agreed to supply the study drug
- Fresenius has been asked to supply ONS
- Approvals is to be obtained
- Awaiting response to applications for funding

Thank you for your attention



St. Olavs Hospital – Trondheim university hospital (foreground)