1

PRC

A feasibility study of Multimodal Exercise/Nutrition/Anti-inflammatory treatment for Cachexia – the pre-MENAC study

Trude Balstad,Clinical nutritionist, PhD
Dept of Cancer Research and Molecular Medicine, Faculty of Medicine, NTNU

2

Definition and classification

Cancer Cachexia:

"multifactorial syndrome defined by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that

cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment.

Its pathophysiology is characterised by a negative protein and energy balance driven by a variable combination of reduced

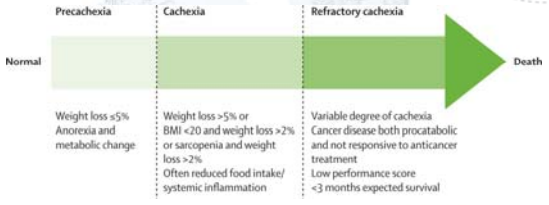
food intake and abnormal metabolism"

Fearon K, *et al*. Definition and classification of cancer cachexia: An international consensus. Lancet Oncology 2011

3

Definition and classification

Stages of cachexia



Fearon K, *et al*. Definition and classification of cancer cachexia: An international consensus. Lancet Oncology 2011

4

Treatment

- No consensus how to treat
- Need to treat early in the trajectory of cachexia
- Single drug agents have been tested
- Nutrition

Fearon K, *et al*. Cancer Cachexia: Developing multimodal therapy for a multidimensional problem. European Journal of Cancer 2008

5

MENAC studies

- Pre-MENAC- study
  - Phase II multicentre study (feasibility study)
- MENAC- study
  - Phase III randomised multicentre study

6

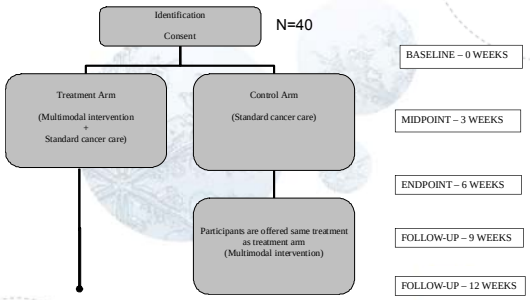
Intervention

Combination of:

- Physical exercise program (restistance/endurance)
- Nutritional supplements (EPA) and advise
- Anti-inflammatory treatment with celecoxib

7

Study schematic



8

Primary objectives

Feasibility of multimodal intervention:

- Enrolment rate
- Compliance with study intervention, study procedures and data collection
- Contamination-rate in the control group with respect to any of the interventions in the intervention group
- Provide an estimate of the sample size required in futures studies in cachexia

9

Secondary objectives

Usefulness of proposed outcome measures:

- Can the intervention stabilise or improve skeletal muscle mass?
- Can the intervention improve or stabilize physical function?
- Can the intervention improve or stabilize nutrition?
- Can the intervention reduce fatigue?
- Does the intervention improve overall survival?

10

Inclusion

- **Main eligibility criteria**
  - Advanced non-small-cell lung cancer (stage III-IV) or pancreatic cancer not eligible for curative therapy
  - Due to commence chemo- or chemo radiotherapy
  - Karnofsky Performance Score ≥ 70
  - 18 –75 years of age
  - A life expectancy of ≥4 months and considered able to complete the study

11

- Neuro-endocrine pancreatic cancer
- Renal impairment (serumalbumin < 25 g/L or Child-Pugh ≥10), creatinine clearance <30ml/min (estimated using cockroft-gault, creatinine measured within two months of date of consent)
- Receiving parenteral nutrition or enteral nutrition via feeding tube
- Weight loss >20% over the previous 6 months
- BMI >30 kg/m2
- Severe anorexia (less than 50% pre-illness food intake and unable to take oral supplements)
- Use of appetite stimulants (such as megestrol acetate, progestational agents, growth hormone, dronabinol, marijuana or other anabolic agent) within 30 days prior to study baseline
- Concomitant long term steroid treatment (inhaled, optical or pulsed oral steroids (up to 10 days use) are permitted).
- Concomitant long term NSAID or Aspirin treatment.
- Regularly scheduled on kinase inhibitors (e.g. sorafinib)
- Women during pregnancy, breastfeeding or who are in child-bearing age and do not use adequate contraception
- Positive history of heart disease, i.e., severe (New York Heart Association Functional class III or IV) heart failure, uncontrolled hypertension (diastolic blood pressure >95 mmHg at screening), history of previous myocardial infarction, unstable angina, coronary revascularization, uncontrolled arrhythmia, and cerebrovascular accident
- Previous gastrointestinal inflammatory disease and history of gastrointestinal ulceration
- History of bronchospasm, asthma, rhinitis, nasal polyps, angioneurotic oedema or urticaria with intake of NSAID or aspirin therapy
- History of hyper sensibility related to intake of acetylsalisylsyre or NSAIDs, including COX-2 (cyklooksygenase-2) inhibitors.
- History of hyper sensibility to Sulphonamides
- Ongoing/planned radiotherapy during the study period affecting the gastric/oesophagus area
- No systemic cancer-treatment last 4 weeks prior to inclusion in the study

12

Registrations

FLOW CHART OF STUDY REGISTRATIONS

Assessment	Baseline (wk -2 to 0)		Midpoint (wk 3)	Endpoint (wk 6)	Follow-up (wk 9)	Follow-up (wk 12)
Patient and Disease Specific Information	X					
Medication last 24 hours	X			X		
Weight	X		X	X	X	X
Death			X	X	X	X
Continued participation			X	X	X	X
Hospitalisation			X	X	X	X
Tolerance of anti-cancer treatment			X	X	X	X
Performance Status Score	X		X	X	X	X
Current level of physical activity	X			X		
Physical activity (ActivPAL)	X			X		X
Physical capacity (6 MWT)	X			X		X
Grip strength (dynamometry)	X			X		X
EORTC QLQ C-30	X		X	X	X	X
Nutrition interview including 24 h recall, PG-SGA and Ave5	X	START OF CHEMOTHERAPY	X*	X	X*	X*
CT scan all tumour lesion + L3 vertebrae	X **			X		X***
Fatigue Severity Scale	X			X		
Blood Samples	X			X		
Compliance			X	X	X	X
Response to anti-cancer treatment				X	X	X
Toxicity (CTC)			X	X	X	X
Patient diary (ONS, celecoxib use, record of activity	Daily		Daily	Daily	Daily	Daily

* PG - SGA and Ave5 only, ** not > 4 weeks prior to start of chemotherapy, *** Optional

13

Trial Centres

- Department of Oncology and Department of Internal Medicine, St. Olav University Hospital in Trondheim, Norway
- Department of Oncology, Oslo University Hospital, Norway
- Beatson West of Scotland Cancer Centre, Glasgow, UK

14

Protocol Development Group

Principal investigators:
Stein Kaasa, professor MD
Department of Cancer Research and Molecular Medicine, Medical Faculty, Norwegian University of Science and Technology, Trondheim, Norway
St.Olavs University Hospital, Department of Cancer, Trondheim. Norway
Ken Fearon, professor MD
Clinical and Surgical Sciences (Surgery), University of Edinburgh, Royal Infirmary of Edinburgh, 51 Little France Crescent, Edinburgh, EH16 4SA, UK

Co-investigators and collaborators:
Tora Skeidsvoll Solheim, MD, Phd Student
Department of Cancer Research and Molecular Medicine, Medical Faculty, Norwegian University of Science and Technology, Trondheim, Norway
St.Olavs University Hospital, Department of Cancer, Trondheim. Norway
Barry J A Laird, MD
Clinician Scientist and Consultant in Palliative Medicine
European Palliative Care Research Centre, NTNU, Norway.
Beatson West of Scotland Cancer Centre and Edinburgh Cancer Centre, UK
Bjørn – Henning Grønberg, MD, post doc
Department of Cancer Research and Molecular Medicine, Medical Faculty, Norwegian University of Science and Technology, Trondheim, Norway
St.Olavs University Hospital, Department of Cancer, Trondheim. Norway
Trude Rakel Balstad, clinical nutritionist, post doc
Department of Cancer Research and Molecular Medicine, Medical Faculty, Norwegian University of Science and Technology, Trondheim, Norway
Nina Aass, professor MD
Regional Centre for Excellence in Palliative Care, Oslo University Hospital, Ullevål, Oslo, Norway
Asta Bye, clinical nutritionist, senior researcher
Regional Centre for Excellence in Palliative Care, Oslo University Hospital, Ullevål, Oslo, Norway
Tone Ikdahl, MD
GI and Uro Oncology Unit, Department of Oncology, Oslo University Hospital, Ullevål, Oslo, Norway
Guro Birgitte Stene, physiotherapist, Phd student
Department of Neuroscience/Cancer Research and Molecular Medicine, Medical Faculty, Norwegian University of Science and Technology, Trondheim, Norway
Sveinung Sørhaug, MD,
St.Olavs University Hospital, Department of Pulmonology, Trondheim. Norway
Tore Amundsen, MD,
St.Olavs University Hospital, Department of Pulmonology, Trondheim. Norway

External experts and collaborators:
Vickie Baracos, MD, professor
Department of Oncology, Division of Palliative Care Medicine, University of Alberta, Edmonton, Canada
Florian Strasser, MD, Ass. Professor
Oncological Palliative Medicine, Division of Oncology/Hematology, Department of Internal Medicine and Palliative Care Center, Cantonal Hospital, Switzerland
Peter Fayers, supervisory study statistician
University of Aberdeen School of Medicine and Dentistry/NTNU Institute of Applied Health Sciences, Aberdeen AB25 2ZD, Scotland

15

PRC

You are welcome to join us for the phase III multi centre study

NTNU – Trondheim Norwegian University of Science and Technology
ST. OLAVS HOSPITAL TRONDHEIM UNIVERSITY HOSPITAL
Kreft
EAPC