

## **To which extent is cancer cachexia syndrome reversible under successful anticancer treatment? An analysis of data in pancreatic cancer patients**

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### **Introduction**

Cancer cachexia syndrome CCS is frequent in advanced solid tumour patients, especially in pancreatic cancer, and is causing a high burden of morbidity and mortality in affected ones. CCS is an independent prognostic factor of the course of underlying malignant disease. It is expected that CCS can improve under successful anticancer treatment as the pathophysiologic mechanisms of weight loss is catabolic drive caused by the cancer itself. Since in pancreatic cancer patients, efficacy of anti-cancer treatment on survival and response rate is relatively poor, the endpoint improvement of weight and physical function is often cited by clinicians to be the main argument for anti-cancer treatment.

### **Aim**

The aim of this study was to review the effect of anticancer treatment on CCS in advanced pancreatic cancer patients.

### **Method**

A systematic review of intervention trials investigating chemo- or chemo-radiotherapies was performed, tested in advanced pancreatic cancer patients, irrespective of whether additional operation was done. We were searching PubMed for all phase III clinical trials which were published between 2000 and 2009 in one of the following journals: Journal of Clinical Oncology, European Journal of Cancer, Annals of Oncology, Journal of Clinical Oncology, Journal of the American Medical Association and Cancer. The following data was extracted: Weight assessment at baseline and over time, weight as trial end point, extent of weight response associated with anticancer treatment, mentioning of CSS assessment and standard management in addition to anti-cancer treatment, discussion of weight in the result and/ or in the discussion sections.

### **Results**

18 interventional trials were identified and reviewed. All except one trial were including weight assessment in the methodology. 14 trials were including change of weight in their results and/or discussion. In 8 studies weight assessment was part of clinical benefit (CB) as one of the trial composite endpoints (including the factors pain, performance status (PS) and weight) but not mentioned independently.

9 trials showed a new effective treatment option. Of those, one study showed a slight increase in average body weight under the successful treatment regimen. Another trial showed a prolongation of the time to body weight reduction under successful anticancer treatment. In 2 trials the benefit of the treatment was based on CB, in 1 of those CB was the only benefit but weight change (increase, stabilisation) was not especially mentioned.

One trial showed an improved weight gain under the more effective old therapy regimen compared to the investigational one.

In no one of the trials favourable weight development was observed in the absence of tumour response. One study mentioned that deterioration of PS and weight were the only indication of disease progression.

In all trials there was no information about the standard basic cachexia management of participants.

**Discussion**

This is the first systematic review exploring improvement of weight loss associated with anticancer treatment in advanced pancreatic cancer patients. Favourable weight development (weight gain, stabilisation or delay in weight loss) was observed as part of the positive effects of successful anticancer treatments.

In addition to weight loss as a prognostic factor, change of weight seems to be a useful single parameter as an endpoint (at least secondary) to assess a substantial treatment efficacy in phase III interventional trials. This review shows that to date this was not commonly done although it is an investigation which is not invasive, inexpensive and assessed almost always anyway and values available.

These results suggest that for any anti-cachexia intervention the control of tumor needs to be defined.