Reviewer's report

Title: Emerging markers of cachexia predict survival in cancer patients

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Reviewer: Athanasios Kotsakis

Reviewer's report:

This is a manuscript investigating 3 peptides ghrelin, obestatin and leptin as prognostic biomarkers of cachexia and overall survival in cancer patients. Blood samples from 140 patients were collected at baseline and after 18 months and analyzed with ELISA for the expression of the above mentioned hormones. Their levels were correlated with the presence of other comorbidities as well as, with the patients' survival. However, there are some major and minor comments.

Major comments:

1) It is not clear what is the novelty of the present study and that should be mentioned and emphasized in the text. What was the primary endpoint and do the results confirm the authors’ assumption? That should be mentioned in the conclusion paragraph.

2) As the authors state, one of the major limitations of the study is the heterogeneity of the patient population. It would be very interesting if more details could be provided regarding the association of the hormone- levels and disease stage, tumor burden defined as number of metastatic sites (subanalyses). Is there any difference between the patients in the adjuvant setting compared to those with stage III or IV disease?

3) Is there any impact of chemotherapy on the hormone- levels?

4) What about the patients who did respond to the treatment? Did the hormone levels return to the normal limits?

Minor comments:

1) In the exclusion criteria reported that patients with congestive heart disease (CHD) or chronic renal failure (CRF) are excluded. However, in the analysis of the data, it is stated that patients with CHD and CRF were included in the study. Please clarify and make clear which are the limits of mild or severe CHD or CRF.

2) Line 49: "Backgroung", please change to Background

3) Table 2: "alkilant agents" please change to alkylating agents and in the same table "ormonotherapy" to hormone therapy

4) Line 208: ".....showed a faster decline of general condition". What is the definition of general condition? Is there any impact of chemotherapy for example?

5) Line 210: "....worse outcomes.....". What is the "worse outcomes"? Please clarify.
6) Were all patients newly diagnosed with cancer? Had all the samples been collected before any medical intervention?

7) The percentages following the chemotherapeutic agents are not very understandable; for example, Platinum 59 (42%), 48 (81%), 11 (9%), where do they refer to?

I believe that the major need of the present study is to make clear if these hormones could be used as prognostic marker at least, in a subgroup of the population included in the study. To this direction, some subanalyses might be needed. If these results are important, I think the study could be accepted for publication.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests