Reviewer’s report

Title: A phase II trial of personalized peptide vaccination in castration-resistant prostate cancer patients: Prolongation of prostate-specific antigen doubling time

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Reviewer: GILBERTO FILACI

Reviewer’s report:

Major Compulsory Revisions

1) The manuscript reports on immunological and clinical results of a clinical trial performed in patients with castration-resistant prostate cancer treated with a personalized peptide vaccine. Although the topic is of great interest, the modality of data presentation does not allow to reach clear conclusions. In fact, in this study several variables are mixed together such as: stages of disease, type and number of administered peptides, number of immunizations, patient's HLA haplotypes. The only stratification made by the authors is the classification of patients in "responder, non-responder and others" based on arbitrary clinical criteria. In particular, the stage of disease should represent a main stratification principle, since changing the dimension of tumor burden and the diffusion of the tumor may radically change the possibility for the immune system to counteract tumor growth. Indeed, overall survival is remarkably different in patients with or without metastasis, as well as in patients who have already received or not chemotherapy. Moreover, PSA level and PSADT may directly depend on the tumor burden. Hence, data should be completely re-analyzed showing the frequencies of vaccine-specific immune responses, PSA and PSADT changes, as well as overall survivals in patients categorized in relationships with their clinical characteristics (i.e., having or not metastases, having or not received chemotherapy, having or not responded to the chemotherapy).

Minor Essentials Revisions

1) Although the authors assess that there were differences in the titers of vaccine-specific antibodies among the three groups they identified, Figure 1A does not show any statistically significant difference. Please, explain, being consistent between text and figures.

2) Although the take-home message is that PSADT is affected by cancer vaccination, the means of PSADT in groups subdivided in relation to achievement or not of immunological or clinical responses are not shown (only elaborations, as percentages of PSA changes and folds of PSADT variations, are presented). Please, show PSADT means of the different groups of patients.

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 disclosure that I'm stock-holder of a small company that applied for a patent related to a peptide cancer vaccine.