Reviewer's report

Title: Alpha-type-1 polarized dendritic cell-based vaccination in recurrent high-grade glioma: A phase 1 clinical trial

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Reviewer: Hideho Okada

Reviewer's report:

The authors describe their experience in conducting a phase I study of vaccination in 9 patients with recurrent high grade gliomas using alpha-type-1 DCs. Although the report could be valuable in the literature, there are numbers of moderate to major issues that hamper the enthusiasm for this manuscript.

Major compulsory revisions

• It has been extensively reported that DC vaccines are generally safe. Therefore, safety of DC administrations in a relatively short-term follow-up is not necessarily novel. Now, they claim they used alpha-type-1 DCs that were originally described by Dr. Kalinski's group. However, it is unclear how “alpha-type-1 DC” are defined, manufactured and validated (see specific issues).
• The manuscript needs extensive linguistic revisions/edits.
• Overall, the manuscript has a number of quality issues in terms of how the results, such as immune response data, were evaluated and interpreted (see below for some of the specific points)

Specific Issues (these are also major compulsory):

• It is entirely unclear how the criteria for positive response were set for immunological assays, such as ELISPOT. Only laboratory procedures for ELISPOT assays were described in the material and method section. However, information is missing as to how the responses were evaluated and determined positive or negative; specifically: 1) when blood samples were drawn: 2) which post-vaccine time point(s) were used to compare with pre-vaccine samples; 3) what were the criteria for calling positive/negative? Similarly, it is unclear how Th1/Th2 was determined (criteria).
• The abstract and background sections start talking about GBM, but the manuscript describes not only GBM but high grade gliomas. Hence, the beginning of these sections seems out of place. Perhaps the authors can revise to talk about high grade gliomas in general with some emphasis on GBM.
• Similarly, there are no clear criteria determining DC1 vs DC2. The authors probably used a method previously described by others (CD11c+HLA-DR-based method?), but there are no clear citations of those previous studies, either.
• Which patient demonstrated liver toxicity? – time relationship to the vaccine
administration?

• Eligibility- was the use of corticosteroid allowed? – is so, how much?

• Some conditions in the exclusion criteria do not seem to belong there: i) prior therapy less than 4 weeks before trial entry (one could just wait rather than calling “ineligible”); vi) anaphylaxis (did the authors mean “previous history of anaphylaxis”?)

• The method section for DC preparation does not include the use of additional cytokines (other than GM and IL-4), while the other sections mention other cytokines to induce “type-1” phenotype.

• Immunohistochemistry for the antigens is not convincing. Can the authors provide pictures with higher magnification showing that tumor cells, but not infiltrating stroma or immune cells, are positive for the antigens?

• It is not clear why “recovery rate” is important. Please provide a better discussion for the rationale for evaluating this.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

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

**Declaration of competing interests:**

I have no relevant conflicts of interests.