Reviewer's report

Title: Serum levels of soluble programmed death-ligand 1 (sPD-L1) in patients with primary central nervous system diffuse large B-cell lymphoma

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Reviewer: Outi Kuittinen

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Comments:

1) Abstract raw 8: They should write PD-1 protein instead of PD-1

2) Introduction should be shorter

3) Authors claim in the introduction that measuring sPD-L1 protein could substitute surgical biopsy. However, sPD-L1 can be elevated in healthy controls as well, and demonstrating elevated serum level can not substitute diagnostic biopsy, even though, according to their results, it can give more precise prognostic information than PD-L1 immunohistochemistry.

4) Materials and methods: Authors do not give any description about the control cases, how they were selected, what was their age, sex distribution etc.

5) Authors have not performed EBV stainings. Because EBV positivity is known to be associated with elevated PD-L1 expression in PCNSL, integrating this information to the data would be essential before drawing definitive conclusions. Also they should describe whether patient were immunocompetent or were there any patients with known immunosupression

6) Discussion: In results authors presented that tumor PD-L1 expresion did not have statistically significant association with outcome. This is in line with previous publications. They found that sPD-L1 correlated with survival. However, in discussion they claim that that sPD-L1 is a surrogate marker for tumor cell PD-1 expression, which in turn, is prognostic for survival. I think it is not possible to draw this kind of conclusion from this study, even though there were some correlations between tissue PD-L1 expression and sPD-L1. There may be other interfering issues, why soluble protein is prognostic, but tumor expression is not. Authors should discuss about that.

In general this is an interesting work stydying the basic biology behind IOL therpies, which in future clearly have a role in the treatment of PCNSL as well. The study has a moderate sample size in such a rare disease. Authors have made a large number of serum cytokine analyzes in combination with tumor sample immunohistochemistry (IHC). IHC results are analyzed separately in different cell types to gain proper information. However I would miss some more detailed data concerning patients immunology. Also, I would not fully agree with the some of the conclusion drawn from the study.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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