

## **Author's response to reviews**

**Title:** Primary bilateral adrenal B-cell lymphoma associated with EBV and JCV infection

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**Author's response to reviews:** see over



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To the Editors-in-Chief of  
*Infectious Agents and Cancer*  
Franco M. Buonaguro (Italy)  
George K. Lewis (United States)  
Pier Giuseppe Pelicci (Italy)

RE: MS: 1156477981221650

Manuscript title: **“Primary bilateral adrenal B-cell lymphoma associated with EBV and JCV infection”**

Authors: L Barzon, M Trevisan, F Marino, V Guzzardo, G Palù

Dear Editors,

We are submitting a revised version of the above manuscript, which has been modified according to the comments and suggestions of the Reviewers. We would like to thank the Editors and Reviewers for their suggestions, which allowed us to improve our work.

A point-by-point response to the concerns of the Reviewers is given below:

**Reviewer number 1:**

*Major Compulsory Revisions*

Besides the presence of JCV in both lesions and the absence in other tissues, it is intriguing the JCV low copy number. Obviously it could have been relevant to know in which cells JCV is present, which viral sequences are expressed, where JCV proteins are. This data would have contributed to define whether the JCV sequences are present in the lymphoma stem cells and/or in bystander cells, and to further characterize the role of JCV in lymphoma pathogenesis.

**Both immunohistochemical staining and western blot analysis of JCV T Ag expression were performed, but with negative results probably because of the relatively low number of JCV-positive cells and the poor quality of tissue samples. The results of these tests have now be added in the text, page 4, bottom.**



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*Minor Essential Revisions*

Minor revisions should be made through out the text to improve expression style and clarity: i.e. instead of "we demonstrated the presence of both EBV and JC polyomavirus (JCV) DNA in" it should be used the expression "the presence of both EBV and JC polyomavirus (JCV) DNA has been detected in".

**The sentence has been modified and the manuscript revised, as suggested.**

**Reviewer number 2:**

1. Major Compulsory Revisions: none

2. Minor Essential Revisions:

The article by Barzon et al. contains the interesting observation of the simultaneous presence of EBV and JCV in a primary adrenal B-cell lymphoma. Although it does not provide direct evidence for a causal relationship between viral infection and tumour development, it is an important contribution to the hypothesis that JCV might provide a synergistic trigger to the oncogenic EBV in B-cell transformation.

The observation was a casual event or the result of a specific investigation aimed to identify the causative agent of primary adrenal B-cell lymphoma? The authors are invited to readdress their working hypothesis.

**The observation was the result of a specific investigation aimed to identify whether potential oncogenic viruses were associated with the lymphoma, as now specified in the text, page 3, line 14 from top.**

The hypothesis that JCV might act as co-factor of EBV in B-cell transformation is well described although the detection of a very low JCV titre: about 0.1 genome copy per cell is unexpected in a high replicating virus like JCV.

**A comment on the low JCV DNA load in tumor tissues has been added in discussion, at page 5, line 18 from top.**

The conclusive phrase of the abstract should be modified as follow "The presence of both EBV and JCV genome sequences suggests the relevance of EBV and JCV coinfection in the pathogenesis of this rare form of B-cell lymphoma."

**The abstract has been modified as suggested.**

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We are looking forward to hearing from you, hoping the manuscript is now suitable for publication in *Infectious Agents and Cancer*.

Sincerely yours,

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