Author's response to reviews

Title: Immunohistochemical and other prognostic factors in B cell non Hodgkin lymphoma patients, Kampala, Uganda

Authors:

Lynnette K Tumwine (tumwinelynette@yahoo.com)
Claudio Agostinelli (claudioagostinelli@gmail.com)
Cristina Campidelli (cristinacampidelli@gmail.com)
Emmanuel Othieno (othienoemma@yahoo.com)
Henry R Wabinga (hwabinga@med.mak.ac.ug)
Simona Righi (pieri@aosp.bo.it)
Brunangelo Falini (faliniem@unipg.it)
Pier Paolo Piccaluga (pierpaolo.piccaluga@unibo.it)
Wilson Byarugaba (wbyarugaba@yahoo.co.uk)
Stefano A Pileri (pileri@aosp.bo.it)

Version: 5 Date: 4 October 2009

Author's response to reviews: see over
Response to reviewers’ comments:

MS: 2028440611291453

Immunohistochemical and other prognostic factors in B cell non Hodgkin lymphoma patients, Kampala, Uganda

Lynnette K. Tumwine¹*, Claudio Agostinelli², Cristina Campidelli², Emmanuel Othieno¹, Henry Wabinga¹, Simona Righi², Brunangelo Falini³, Pier Paolo Piccaluga², Wilson Byarugaba¹, Stefano A. Pileri²

Response to reviewers’ comments:

Dear Ann,
Thank you very much for your email asking us to address the reviewers’ comments on our manuscript. Here is a detailed response to the comments. In addition we have reformatted figure 1 to make it clearer to the readers.

1. Response to Dr. Yasufumi Masaki comments

We thank this reviewer very much for the constructive and helpful comments. We agree that this paper brings out some differences between B cell non Hodgkin lymphomas in developed countries and developing countries. A very good example is that the commonest B cell non Hodgkin lymphomas in developed countries are diffuse large B cell lymphomas.

However in tropical developing countries, the commonest B cell non Hodgkin lymphoma is Burkitt lymphoma.¹ Hence the finding in this paper that the majority of B cell non Hodgkin lymphomas in Uganda (a developing country) were Burkitt lymphomas is not surprising.

In our previous paper, we found that CD30 positivity was high (37%) among Burkitt lymphoma patients in Uganda¹. This was different from findings in developed countries where CD30 positivity in Burkitt lymphoma patients is not so high; for example Jones and others found 18% (3/17) CD30 positivity in childhood Burkitt lymphoma in the West Midlands, in the UK.² Several authors have suggested that the CD30-CD30L interaction may have a role in some non Hodgkin lymphomas including BL.³ ⁴Kanavaros et al 1992 found that many CD30 positive non Hodgkin lymphomas (NHLs) were EBV positive.⁵

These changes have been made on page 10 of the revised manuscript.
In our patients, CD30 positivity was found among those with both “typical morphology and plasmacytoid features.” As we said in our previous paper, this might be related to the “postulated complex pathogenesis of BL” in Africa. Of interest is the multistep oncogenetic mechanism (proposed by Klein “in which there is de-regulation of MYC gene and subsequent development of a malignant clone.” However more studies are needed to be able to understand the specific role of CD30 in Burkitt lymphomas.

Please note that all these changes have been effected in the manuscript on page 10.

**EBV results**

We inadvertently omitted the EBV results. Overall 97.3% were EBER positive. Survival information was available on 25 patients whose EBER results were available. Of these, 24 (96%) were EBER positive. The mean survival for the 24 was 9.28(95%CI 3.27-15.29 months). However there was only one EBER negative patient whose survival was 1.2 months.

55 cases had both CD30 and EBER results. Of the 24 CD30 positive, 23(95.8%) were EBER positive. Of the 31 CD30 negative, 30(96.8%) were EBER positive. The difference was not statistically significant (p=0.83); and because of this, EBER result was not entered into Cox regression analysis.

These results have been reflected in the revised manuscript on page 8.

---

2. **Response to Uma N Sundram comments**

We are grateful to the reviewer for these comments.

Ann, let me thank you once again for having given me the opportunity to submit my manuscript online and respond to the reviewers’ comments accordingly. It has been a very positive and enriching experience.

Lynnette K. Tumwine
1. Tumwine L, Campidelli C, Righi S, Neda S, Byarugaba W, Pileri S. B-cell non-Hodgkin lymphomas in Uganda: an immunohistochemical appraisal on tissue microarray. *Hum Pathol* 2008; 39(6):817-823.

2. Jones T, Coad N, Muir K, Parkes S, Evans C, Mann J. Immunophenotypic analysis of childhood Burkitt's lymphoma in the West Midlands 1957-1986. *J Clin Pathol* 1995; 48: 2225.

3. Gruss H, Boaini N, Williams D, Armitage R, Smith C, Goodwin R. Pleiotropic effects of the CD30 ligand on CD30-expressing cells and lymphoma cell lines. *Blood* 1994; 83(8):2045-2056.

4. Horie R, Watanabe T. CD30: expression and function in health and disease. *Seminars in Immunology* 1998; 10(6):457-470.

5. Kanavaros P, Jiwa N, De Bruin P, et al. High incidence of EBV genome in CD30-positive non- Hodgkin's lymphomas. *the Journal of Pathology* 1992; 168(3):307-315.

6. Van den Bosch C. Is endemic Burkitt’s lymphoma an alliance between three infections and a tumour promoter? *The Lancet Oncology* 2004; 5: 738-746.

7. Klein G. Lymphoma development in mice and humans: diversity of initiation is followed by convergent cytogenetic evolution. *Proc Natl Acad Sci USA* 1979; 76: 2442-2446.