Impact on survival through consolidation radiotherapy for diffuse large B-cell lymphoma: a comprehensive meta-analysis

Martin D. Berger, 1* Sven Trelle, 2* Annina E. Büchi, 3 Sabrina Jegerlehner, 3 Codruta Ionescu, 4 Thierry Lamy de la Chapelle 5 and Urban Novak 1

¹Department of Medical Oncology, Inselspital, Bern University Hospital, University of Bern, Switzerland; ²CTU Bern, University of Bern, Switzerland; ³Department of General Internal Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; ⁴Department of Radiation Oncology, Inselspital, Bern University Hospital, University of Bern, Switzerland and ⁵Hematology Department, Rennes University Hospital, INSERM Research Unit 1236, Rennes, France

*MDB and ST contributed equally as co-first authors.

©2021 Ferrata Storti Foundation. This is an open-access paper. doi:10.3324/haematol.2020.249680

Received: February 9, 2020. Accepted: June 12, 2020. Pre-published: June 18, 2020.

Correspondence: URBAN NOVAK - urban.novak@insel.ch

"Impact on survival through consolidation radiotherapy for diffuse large B-cell lymphoma: a comprehensive meta-analysis" by Berger et al.

Supplemental material

SUPPLEMENTAL INFORMATION ON THE STATISTICAL ANALYSIS

All meta-analyses were done using a random-effects model. Between-trial heterogeneity τ^2 was estimated using the method proposed by Paule and Mandel¹ and as implemented by the empirical Bayes option of the metareg command in Stata.² Confidence intervals were calculated as suggested by Knapp and Hartung³ and prediction intervals as suggested by Higgins et al.⁴ Timetrend and stratified analyses were done using the same methods. Bivariate meta-analysis was done using the mvmeta command in Stata (White 2009 and 2011).^{5,6} If HR and a measure of precision (standard error, variance, or confidence interval) was not available, we digitized Kaplan-Meier curves, reconstructed the underlying time-to-event data, and calculated (log) HRs and standard errors using a Cox regression model.⁷ Correlation between progression-free and overall survival within the two trials included in the meta-analysis^{8,9} that provided sufficient data was calculated by Spearman's rank correlation coefficient. A between-outcome correlation of 0.8 was finally used. Sensitivity analyses showed robustness of the analysis.

Table S1: Current ESMO and NCCN guidelines on consolidation radiotherapy for DLBCL

Compilation of the current guidelines of ESMO (Tilly, 2015)¹⁰ and NCCN (National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: B-cell lymphomas, version 6.2019: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf (Accessed Nov 28, 2019)) on the use of the consolidation radiotherapy for patients with DLBCL.

Society	Indication	No indication	Unclear
ESMO	Young, low risk, aaIPI 0, bulky disease (R-CHOP)	Young, low risk, aaIPI 0, non-bulky disease	Young intermediate to high risk (aa-IPI \geq 2)
NCCN	Consider in stage I&II, (non)bulky, partial response or EoT PET+	When a complete response is achieved	no firm indication

References

- ¹ Paule RC, Mandel J. 1982. Consensus values and weighting factors. National Institute of Standards and Technology.
- ² Habord RM, Higgins JPT. 2008. Meta-regression in Stata. Stata Journal 8: 493-519.
- ³ Knapp G, Hartung J. 2003. Improved tests for a random-effects meta-regression with a single covariate. Stat Med 22: 2693-2710.
- ⁴ Higgins JP, Thompson SG, Spiegelhalter DJ. 2009. A re-evaluation of random-effects meta-analysis. J R Stat Soc Ser A Stat Soc 172: 137-159.
- ⁵ White IR. 2009. Multivariate random-effects meta-analysis. Stata Journal 9: 40-56.
- ⁶ White IR. 2011. Multivariate random-effects meta-regression: Updates to mymeta. Stata Journal 11: 255-270.
- ⁷ Guyot P, Ades AE, Ouwens MJ et al. 2012. Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan-Meier survival curves. BMC medical research methodology 12: 9.
- ⁸ Reyes F, Lepage E, Ganem G, et al. 2005. ACVBP versus CHOP plus radiotherapy for localized aggressive lymphoma. N Engl J Med 352(12): 1197-205.
- ⁹ Bonnet C, Fillet G, Mounier N, et al. 2007. CHOP alone compared with CHOP plus radiotherapy for localized aggressive lymphoma in elderly patients: a study by the Groupe d'Etude des Lymphomes de l'Adulte. J Clin Oncol 25(7): 787-92.
- ¹⁰ Tilly H, Gomes da Silva M, Vitolo U et al. 2015. Diffuse large B-cell lymphoma (DLBCL): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 26 Suppl 5: v116-125.