To the editor:

SNP rs6457327 is a predictor for overall survival in follicular lymphoma as well as survival after transformation

Follicular lymphoma (FL) is one of the most common types of B-cell lymphoma. Patients with FL follow an indolent clinical course but eventually succumb to the disease. Follicular lymphoma commonly transforms to the more aggressive diffuse large B-cell lymphoma (DLBCL) at a frequency of 10-60%.[1]

In a recent paper by Wrench et al, it was shown that the SNP rs6457327 is a predictive marker for the transformation of FL to DLBCL.[2] The aforementioned study reported an increased risk of transformation as well as a shorter time to transformation in carriers of the A-allele (AA or AC genotype) compared with patients homozygous for the C-allele ($P < .01$).

Complementing this comprehensive study, we analyzed the rs6457327 SNP using the PCR-RFLP method in a cohort of 102 FL patients. Front-line treatments were radiotherapy in 36 patients, chlorambucil in 16 patients, CHOP in 19 patients, other regimens in 5 patients and 26 patients with observation only (wait and watch). From these 102 FL patients, 48 patients showed biopsy-proven transformation to DLBCL.

In accordance to the Wrench et al study, we found a higher risk of transformation in carriers of the A-allele ($P = .04$) as well as a trend toward a shorter transformation time in our Swedish material ($P = .15$; data not shown).[2]

However, we found that the patient genotype at this position correlates to overall survival time, measured from the initial FL diagnosis, with a median survival of 9.1 year for AA or AC carriers compared with 11.7 years for the CC patients which, to our knowledge, has not been previously shown ($P = .006$, Figure 1A). We also found that this polymorphism significantly affects the survival time after transformation to DLBCL, with a median survival of 2.2 years for AA or AC carriers compared with 4.9 years for CC patients ($P = .04$; Figure 1B).

Very little is known about the affects and relevance of SNP rs6457327, except that the polymorphism is located in the human leukocyte antigen region (HLA) on the chromosome 6p21.33. An earlier study has also shown that the polymorphism could be responsible for the development of FL, where the A-allele was the risk allele.[3] In the study by Wrench et al it is suggested that the rs6457327 genotype is associated with risk of transformation as well as shorter time to transformation in FL patients.[2] Interestingly, in an earlier study by Flordal-Thelander et al, 3 of 8 transformed DLBCL tumors showed loss of 6p21 and 2 of these involved 6p21.33.[4] The loss of this region occurred only during or after transformation, indicating that genes at 6p21 could be involved in the histologic transformation process from FL to DLBCL.

Because a loss and not a gain of this region were more commonly found, one could speculate that a potential tumor suppressor gene is located at 6p21. Furthermore, the A-allele at rs6457327 could be associated with lower expression of this hypothetical tumor suppressor gene.

In summary, we show that FL patients who later transform to DLBCL have a significantly worse prognosis if they carry the AA or AC genotype compared with those patients carrying the CC genotype at SNP rs 6457327. However, it is necessary to explore the biology behind this finding and it would also be desirable to perform larger studies to confirm this result. This finding could improve prediction of clinical outcome and be helpful in the design of new treatments.

Mattias Berglund
Departments of Oncology, Radiology and Clinical Immunology, Uppsala University, Uppsala, Sweden

Gunilla Enblad
Departments of Oncology, Radiology and Clinical Immunology, Uppsala University, Uppsala, Sweden

Ulf Thunberg
Departments of Oncology, Radiology and Clinical Immunology, Uppsala University, Uppsala, Sweden

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Correspondence: Ulf Thunberg, PhD, Departments of Oncology, Radiology and Clinical Immunology, Rudbeck Laboratory, Uppsala University, SE-751 85 Uppsala, Sweden; e-mail: ulf.thunberg@onkologi.uu.se.

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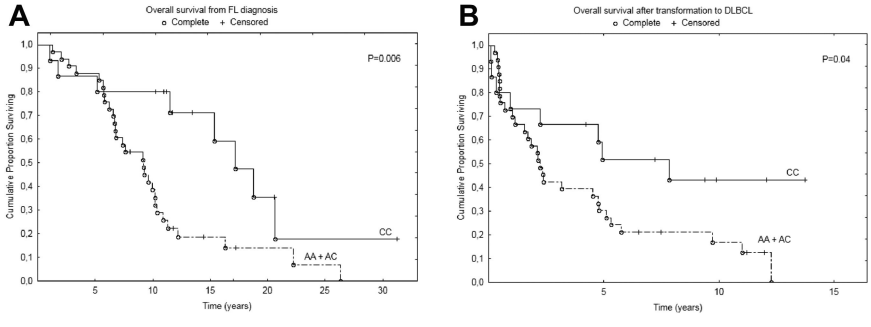

Figure 1. Overall survival time from initial FL and after transformation to DLBCL. (A) Overall survival time from the initial FL diagnosis for patients carrying the AA or the AC genotype compared with patients carrying the CC genotype ($P = .006$). (B) Overall survival time after transformation to DLBCL with patients carrying the AA or the AC genotype compared with patients carrying the CC genotype ($P = .04$).