Reply to "Fc gamma receptor 3a genotype in follicular lymphoma: the end of the story?" Haematologica. 2012;97(11):e45.

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We appreciate the comments from Professor Prochazka and colleagues, and thank them for drawing attention to their experience with the prognostic significance of Fc gamma receptor 3A (FCGR3A) polymorphisms in follicular lymphoma.[1] In our manuscript,[2] we discuss a number of limitations in our study that make the conclusion about the impact of FCGR3A polymorphism on outcomes tentative, much as Prochazka *et al.* concluded themselves. There are studies to support both the presence and absence of significance, but in our study we concluded that evidence favors its significance.

The outcomes between the trials of CHOP followed by rituximab and CHOP followed by tositumomab/iodine 131 tositumomab were similar, which led us to pool the trials. This is supported by a randomized trial of CHOP-rituximab *versus* CHOP-tositumomab/iodine 131 tositumomab, showing similar outcomes, as presented by one of the authors of the manuscript.[3] To date, no comparison of pharmacokinetics between concomitant use of rituximab with CHOP 6 times every three weeks and 4-weekly doses of rituximab has been made, but considering the long half-life of rituximab, they would not be expected to be very different. The impact of rituximab pharmacokinetics on follicular lymphoma outcomes is a subject of investigation.[4]

The trial of CHOP followed by rituximab did not collect data on hemoglobin and sites of lymphnode involvement, so FLIPI scores could not be ascertained, as we pointed out in the manuscript. IPI risk factors were examined and conclusions remained unchanged.

We do refer to an earlier analysis of the SAKK study in our manuscript[5] on the most recent analysis of event-free survival.[6] The comparison of 158V/V *versus* 158V/F or F/F lost its statistical significance on univariate analysis (P=0.079). However, this study of single-agent rituximab followed by rituximab maintenance *versus* observation is not the ideal setting for answering our original question: does addition of anti-CD20 antibody to chemotherapy improve outcomes preferentially for FCGR3A 158V/V and V/F genotypes? A comparison to a chemotherapy-only arm is required. The ideal setting for this study would have been one of the prospective randomized trials of chemotherapy *versus* chemotherapy combined with rituximab. This setting, unfortunately, was not available to us.

In conclusion, we agree with Prochazka *et al.* that our study has limitations that we also acknowledged. However, all patients with CD20-positive lymphomas receive anti-CD20 monoclonal antibodies, and the goal is now to improve the outcomes of poor responders. The development of new anti-CD20 antibodies with a higher affinity for FCGR3A 158F/F testifies to the interest in the topic.

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