Fc gamma receptor 3a genotype in follicular lymphoma: the end of the story? *Reply to* "Fc gamma receptor 3a genotype predicts overall survival in follicular lymphoma patients treated on SWOG trials with combined monoclonal antibody plus chemotherapy but not chemotherapy alone". Haematologica. 2012;97(6):937-942.

We have read with great interest the results of the recently published retrospective analysis of the Southwest Oncology Group (SWOG) trials.[1] This paper will have an extraordinary impact on decision-making in clinical practice worldwide. Persky and colleagues concluded that Fc gamma receptor 3A polymorphism (FCGR3A) status may be predictive of survival in follicular lymphoma patients receiving treatments containing an anti-CD20 antibody. We fully agree with the statement that the exact mechanism of rituximab activity is not completely understood and polymorphisms such as FCGR3A (CD16), expressed on NK cells and macrophages, may result in different ADCC activation and, therefore, obtain different benefits from rituximab. However, we are doubtful about the conclusion that the predictive role of an Fc gamma receptor 3A polymorphism could be applied to all patients treated with an anti-CD20 antibody.

First, the authors analyzed patients with two different treatment strategies using monoclonal antibodies. Thirty of them received CHOP followed by four doses of rituximab and 42 patients were treated with CHOP followed by tositumomab and iodine I 131. Neither regimen is currently standard in the US or Europe[2,3] and they probably have different treatment efficacy. Sequential application of an antibody leads to different pharmacokinetics of the antibody than that in standard concomitant use.

Second, the results may be influenced by the risk of lymphoma. We have no data about FLIPI scores in the CHOP-rituximab arm patients. It would be interesting to confirm the prognostic power of the FCGR3A polymorphism in multivariate analysis with conventional prognostic factors.

Finally, despite the conclusion of the study, some studies did not support the predictive value of the FCGR3A polymorphism in patients treated in the rituximab era. A large prospective trial conducted by the Swiss Group for Clinical Cancer Research (SAKK) showed no differences among FCGR3A in terms of response or survival.[4] Similarly, our results suggested that in patients with advanced follicular lymphoma treated with risk-adapted immunochemotherapy this polymorphism has no prognostic impact.[5]

In conclusion, we believe that results obtained in a limited sample of patients treated with two different regimens are not sufficient to allow a conclusion about the prognostic impact of the FCGR3A polymorphism to be drawn.

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Key words: follicular lymphoma, Southwest Oncology Group, Fc gamma receptor 3A polymorphism, monoclonal antibody, prognosis.

Citation: Fc gamma receptor 3a genotype in follicular lymphoma: the end of the story? Reply to "Fc gamma receptor 3a genotype predicts overall survival in follicular lymphoma patients treated on SWOG trials with combined monoclonal antibody plus chemotherapy but not chemotherapy alone". Haematologica. 2012;97(6):937-942. Haematologica 2012;97(11):e45. doi:10.3324/haematol.2012.071563

The information provided by the authors about contributions from persons listed as authors and in acknowledgments is available with the full text of this paper at www.haematologica.org.

Financial and other disclosures provided by the authors using the ICMJE (www.icmje.org) Uniform Format for Disclosure of Competing Interests are also available at www.haematologica.org.

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